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INFECTIOUS DISEASES

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OXFORD MEDICAL PUBLICATIONS

INFECTIOUS DISEASES

A PRACTICAL TEXTBOOK

BY

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M.D. Ed., F.R.C.P. Ed.

MEDICAL SUPERINTENDENT, CITY HOSPITAL, EDINBURGH, AND LECTURER ON

INFECTIOUS DISEASES TO THE UNIVERSITY OF EDINBURGH

MAJOR, R.A.M.C. T.F.

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PREFACE TO THE SECOND EDITION

THE appearance of this edition, which it had been intended to produce in 1914, has been delayed by the war, and in consequence the greater part of the volume, which at that time was nearly ready for publication, has been subjected twice to thorough revision. The large amount of work which has been done on the subject of infectious diseases during the last ten years has necessitated extensive alterations and additions, and several portions of the book have been entirely rewritten. To make room for new matter the chapter on relapsing fever has been omitted and the sections on bacteriology and pathology have been reduced to the lowest possible limits.

While the book remains for the most part a record of personal experience, it was found impossible during the war to give time to make trial of many forms of treatment and methods of diagnosis which appear well worthy of notice. It has seemed advisable, therefore, to include not a few of which I have little or no practical experience, but which I hope to employ at the first possible opportunity. No doubt there are many unavoidable omissions in the pages which follow, but few, I trust, of outstanding importance.

I have in this edition made use of so many valuable contributions to the literature of the subject that it seems almost invidious to make special mention of a few only of their authors. But I desire to express my particular indebtedness to the writings of Drs. J. D. Rolleston, E. B. Gunson, and Frederic Thomson in this country, and to those of Drs. Charles V. Chapin, Frederick P. Gay, William H. Park, and Abraham Zingher in the United States of America. To the last named, especially, I owe a debt of gratitude both for the instruction he gave us at the City Hospital in the technique of the Schick test and for the coloured plate which illustrates it in this volume.

C. B. K.

EDINBURGH, *April*, 1920.

PREFACE TO THE FIRST EDITION

IN the following pages an attempt has been made to lay before the reader the practical side of the subject under discussion. Bacteriology is to-day so highly specialized that it seemed wiser to barely mention it except in relation to those diseases in which it has a clinical application, and pathology has received no better treatment. But no effort has been spared to do justice to the great questions of diagnosis, prognosis, and treatment, which are, when all is said and done, of most interest both to the student of medicine and to the general practitioner. The volume is not intended to be an exhaustive treatise on the literature of its subject, and references are therefore not given. It is rather a record of personal experience, supplemented as far as possible by information gathered from the best sources and, it is hoped, duly acknowledged.

The Edinburgh City Hospital, admitting as it does to its wards not only all the notifiable diseases but also measles and whooping-cough and, when space is available, even such trivial conditions as rubella, mumps, and chicken-pox, has proved an exceptionally interesting and valuable field for the study of the various infections. Except as regards those diseases which are of rare occurrence, I have relied for the most part upon my own experience, and I trust that this will palliate, if not entirely excuse, the somewhat frequent use of the personal pronoun in the pages which are to follow. There is but little in the volume which has not been already given in the form of bedside instruction. The small number of meetings, however, allotted to the class of infectious fevers and the fact that the teaching given is necessarily determined by the diseases epidemic at the time prevent any single section of students making practical acquaintance with more than a fraction of the subject.

To fill the gaps in their instruction was my primary object in writing this book.

The selection of the illnesses discussed has doubtless been somewhat arbitrary. They are those treated at the City Hospital and on which I feel competent to express an opinion. One exception has been made in the inclusion of relapsing fever, a disease which, owing to its protozoal origin and to its unusual course, appears to possess a special interest which is not lessened in my own eyes by the fact that one of its less known synonyms, 'the epidemic fever of Edinburgh', gives it a sentimental attraction to men of that school.

I have to express my thanks to my friends and former assistants, Dr. J. Halley Meikle, Dr. T. Lauder Thomson, and Dr. Burnet, for the black and white illustrations in the volume. I am also especially indebted to Dr. Foord Caiger, whose extraordinary kindness in allowing the colour photographs to be taken in the South Western Hospital and in selecting the subjects I shall always gratefully remember.

C. B. K.

EDINBURGH, *July*, 1909.

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CHAPTER I

INTRODUCTION

Bacteriology.	The Symptoms of Fever : hyperpyrexia.
Infection.	The Stages of Fever.
The Incubation period.	The Management and Treatment of Fever.
Toxins.	Serum and Vaccine Treatment.
Immunity.	Diet in Fever : in convalescence.
Anaphylaxis.	Diagnosis of Eruptions.
Fever.	Prophylaxis : disinfection.

To discuss bacteriology in relation to the infectious diseases, or to attempt to give any descriptive account of the processes connected with immunity, would be quite foreign to the purposes of a book which concerns itself with the actual state of health of the infected individual. Every student of to-day has ample opportunity of acquiring during his curriculum the main elementary facts connected with both subjects, and the latter in particular, with its complicated experiments and its chaotic terminology, does not lend itself satisfactorily to condensation. It has been proved that many of the diseases to be discussed in the following pages are due to the invasion of the human organism by specific bacteria. It is reasonable to assume that the others, whose etiology still remains obscure, will be found to depend on a similar cause. The infecting micro-organism, however, need not necessarily be a bacterium. Microscopic animal parasites have been proved to be responsible for malaria, and some observers hold that both small-pox and scarlet fever are probably the results of protozoal infection. The spirillum of relapsing fever is also held to be of this nature.

In the early days of bacteriology the difficulties of the subject were hardly realized. Definite morphological differences were found to exist between the micro-organisms which caused the different infections. One was due to a flagellated bacillus, another to a non-motile bacillus, a third to a diplococcus, and so on. And, broadly speaking, these differences in morphology were corroborated by the behaviour of the micro-organisms when cultivated on various media. One grew best upon blood serum, another on nutrient agar ; some caused gas formation in the process of growth, others did not. But, unfortunately for the simplicity of the subject and for its practical

application to everyday medicine by the general practitioner, it soon became obvious that groups of bacteria existed, the similarity of the members of which was so great that the most delicate and prolonged cultural tests were found necessary for their differentiation. Mere morphological characteristics, or staining peculiarities, are not of themselves sufficient evidence of the identity of a particular germ. Important as they are, they have to be considered in conjunction with the character of the growth upon perhaps half a dozen elaborately prepared media, and with the results of the inoculation of small animals. The differentiation of the typhoid group of bacilli, of the diphtheroid group, and of the many varieties of diplococci and streptococci are instances in point. Recently, moreover, it has become evident that certain well-recognized micro-organisms, the meningococcus and the pneumococcus, for example, possess sub-varieties with quite distinct agglutination properties, and that for specific treatment to be successful the curative serum employed requires either to contain antibodies for all the types of the micro-organism or preferably to have been prepared from the particular type which has infected the patient. It may also be mentioned that the behaviour of germs to different cultural tests may vary very much from time to time, and that particular strains of a given bacterium may be trained, so to speak, to acquire such a quality, for instance, as the power to ferment sugar, a capacity which may not under ordinary conditions be possessed by the germ in question. Germs in fact appear to be considerably influenced by their environment, and this naturally raises the question of their mutability, but all attempts to transform one bacterium into another of a closely allied variety appear hitherto to have failed. The clinician, again, may well be puzzled by a recent suggestion that some micro-organisms, as we know them, are merely temporary and perhaps harmless phases in the life history of germs which may be filter-passers and perhaps ultra-microscopic. These bacteriological difficulties make it sufficiently clear that for a really reliable opinion we must have recourse to a skilled bacteriologist who must have all the resources of a well-equipped laboratory at his disposal. Bacteriology is not for the general practitioner, and even a positive report, sent to him from a laboratory within twenty-four hours, does not necessarily mean that his patient, for instance, is suffering from diphtheria, but that an organism, corresponding in its staining properties with the bacillus of that disease, has been successfully isolated from the nose, throat, or ear of his patient. On the other hand, every medical man who possesses an oil-immersion microscope, and has had an elementary course in bacteriology, can gain most valuable indications from the examination of direct preparations, such as a smear from a throat or a cerebro-spinal fluid. I am of opinion, indeed,

that more could be done on such lines than is usually attempted, especially in country practice, where laboratories are not readily available.

INFECTION. By infection is understood the invasion of the tissues by a pathogenic bacterium. And here it may be remarked that it is difficult to draw a hard and fast line between pathogenic and saprophytic bacteria. Many micro-organisms, such as those of typhoid and cholera, are capable of leading a saprophytic existence outside the body, and again certain saprophytes, if introduced in sufficient doses, may be undoubtedly pathogenic. A pathogenic micro-organism, however, may be regarded as one capable of producing disease in man under natural conditions. The effect of its invasion of the human subject will depend upon its virulence, which may vary greatly in different circumstances, upon its dose, which is probably an extremely important factor, and upon the susceptibility of the individual attacked. The latter will differ widely according to the age, race, and personal peculiarities of the infected subject.

All infection must be derived, directly or indirectly, from a patient suffering from the disease or from a healthy individual who, either as the result of an attack of the disease or without having suffered from it, harbours the causative micro-organisms in some part of his body. It is now realized that such a person, who is termed a 'carrier', plays a very important part in the dissemination of several of the infectious diseases, as, for instance, enteric fever, cerebro-spinal meningitis, and diphtheria. Given a source of infection, we have to consider in what manner germs are likely to be transmitted, and with our present knowledge of the bacterial causes of infectious disease it is difficult for us to draw, like our predecessors, fine distinctions between contagion and infection. To-day, thanks largely to the illuminating and suggestive writings of Chapin and of other workers in the same field, we are led to lay more and more stress upon the importance of infection by contact. We use the word *contact* in a very broad sense, not necessarily implying that it is necessary to touch the infecting individual. Chapin defines contact infection as the 'transference of rather fresh infecting material from one to another', and such a definition would include not only those cases of direct contact in which, for instance, a mother contracts diphtheria by kissing a sick child, and of the so-called *droplet infection* in which the infecting individual disseminates germs in his immediate vicinity in the act of sneezing or even talking, but also those cases in which the comparatively fresh virus is carried, perhaps to an adjoining room or house, on the hands or clothes of a nurse or on such articles as spoons, cups, or instruments. This last mode of transference may no doubt be more literally *transmission by fomites*, but the American Public Health Association

has defined that indirect mode of infection as 'spread by means articles which retain the infection for a considerable period of time', and this distinction appears a perfectly logical one. Such fomites would include textile articles, such as bed linen, handkerchiefs, and possibly books. There is little doubt that too much importance has been attached in the past to the transmission of infection by such means. The recent discovery of the part played by 'carriers', and the appreciation of the importance of 'missed cases' of a mild nature in spreading infectious disease have done much to explain instances of infection which would have been formerly attributed to the agency of fomites, and this is to a great extent corroborated by the fact that certain bold experiments in the discarding of disinfection have not been attended with the disastrous results which, only a few years ago, we would have predicted with confidence. Our knowledge of epidemiology advances so rapidly that measures of prevention considered necessary to-day may in a year or two be regarded as entirely superfluous. Chapin reminds us, for instance, that yellow fever, a disease long believed to be disseminated by fomites, has been satisfactorily proved to be insect-borne, and that careful observations have demonstrated that even grossly contaminated clothing and bedding are, from a practical standpoint, quite innocuous. Certain spore-forming and resistant bacteria, however, are undoubtedly capable of being transmitted in this manner and, if we cannot regard infection by fomites as being so universally important as was once believed, it is undoubtedly a mode of transmission with which we still have to reckon in some of the infectious diseases.

Of much more importance is the transference of micro-organisms from the infected individual or healthy carrier through the medium of *water, milk, and various articles of food*. These may have become contaminated by the excretions or the mouth secretions of the infecting person, or the germs may have been carried to food substances by flies. The brilliant results of the campaigns against the mosquitoes responsible for the transmission of malaria and yellow fever, and notably that of Gorgas in the Panama Canal zone, have naturally directed attention to the part played by *insects* in the transference of infection. It is now recognized that our own common house-fly can carry pathogenic bacteria both on its legs and in its alimentary tract. Its free access to food in this country makes it very liable to disseminate such conditions as epidemic diarrhoea and enteric fever. Body vermin, moreover, such as fleas and lice, have been proved to be the principal agents concerned in the dissemination of certain diseases and, like the mosquito, inoculate the virus directly into the individual attacked.

In considering the probabilities of infective micro-organisms being transmitted by *air*, it is well to remember that those who originally regarded certain diseases as air-borne had not our present knowledge of their ordinary mode of transmission, and were therefore reduced to refer them to miasmata, to sewer gas and so forth, and, if these could be excluded, to the free air of heaven itself. It is obvious, then, that we, unaware of what new discoveries regarding common diseases may be awaiting us, should only accept with the utmost caution reports of the apparent transference of their infection by means of air. No doubt 'droplet' infection can be regarded as air-borne for very short distances, but, as pointed out above, it appears to fall more properly under the head of 'contact' infection. Beyond an area in the immediate vicinity of the infectious person it is not now contended that the germs of most of the infectious diseases are transmitted by air even to persons in the same ward. Many competent observers, however, would still claim that aerial transmission plays some part in the transference of the virus of measles and chicken-pox to persons under the same roof, and that notwithstanding the striking success of Rundle in treating these diseases, together with others in the same hospital ward (see p. 601). The question, no doubt, remains an open one, though it must be recollected that it is extremely difficult to make certain that contact infection may not have occurred even in excellently managed wards. As regards transmission in the open air, few nowadays regard it as possible except in the case of small-pox, and even as regards that disease the evidence, as will be seen in a subsequent chapter, is far from conclusive. The question of grossly contaminated *dust* is, however, of importance so far as resistant micro-organisms such as the bacilli of tubercle, diphtheria, and typhoid are concerned. Although experiments by Flüge have suggested that it is impossible to infect animals with dust containing tubercle bacilli, and other observations go to show that it is improbable that inhaled bacteria ever reach the lungs, it is not unreasonable to conclude that such a mode of infection, if rare under ordinary conditions, is at least possible. Again, as regards enteric fever I would range myself with those who consider that infected dust was responsible for many of the cases which occurred in the Boer war, even admitting that transference by flies and contact infection were of greater importance. When we hear of the dried contents of latrines being dispersed over a camp, and incidentally over the food of the men, by dust storms, it is difficult to resist the conclusion that infection could hardly be avoided, though we may grant that the circumstances were exceptional. The great point to remember at present, however, is that our predecessors' confident explanations of the transmission of many diseases have proved hopelessly

wrong, and that it is unwise to make dogmatic assertions about conditions, the bacteriology of which is still uncertain. It is interesting, and this is a point emphasized by Chapin, to note the changed views of the surgeons. Modern surgery was founded on the exclusion of air and dust from the area of the operation. Nowadays contact infection is undoubtedly regarded as of most importance.

Infection takes place in three ways : by *ingestion*, as is usually the case in enteric fever ; by *inhalation*, which we may assume takes place in such diseases as measles and small-pox ; and by *inoculation*, which is the ordinary mode of infection in the insect-borne diseases and in such a condition as erysipelas. Some germs may find their way into the human body by more than one of these routes ; thus the plague bacillus may be inoculated by the bite of the rat-flea or may be inhaled as the result of droplet infection, and the bacillus of tubercle may obtain entrance by any of these three ways. Bacteria produce disease firstly by their multiplication in the body, which may be called 'infection', and secondly by the production of toxins or poisons which may act either generally or locally, 'intoxication'. In some diseases the local effect is the prominent feature, in others the general is more obvious. In certain instances the multiplication of the micro-organisms appears to take place in the blood-stream, but in man it is on the whole unusual to find many bacteria in the blood, though in fatal cases of septicæmia the capillaries may be found after death to contain large numbers of organisms. More usually a local nidus for multiplication is obtained either at the spot first invaded, as, for instance, the fauces in diphtheria, or in some of the other organs of the body, such as the intestinal lymphoid glands and the spleen in enteric fever, to which they may have been carried by the blood-stream.

Whatever may be the exact cause, an interval occurs, after the moment of infection, before the first symptoms of the disease manifest themselves. This latent stage, or period of **incubation**, varies much in length in the different diseases. In some it is very short, in others it may last for weeks. Until recently very little has been done to explain this latency. All that could be said was that time was presumably needed for the establishment of the micro-organisms in the body and perhaps also for developing their power of producing toxins in sufficient quantity to overcome the natural methods of protection of the normal organism. It might also conceivably depend upon bacteriolytic substances, the proteolytic ferments suggested by Vaughan, gradually developed in the body, setting free endotoxins, hitherto inactive, after a certain interval. The most modern theory, that of von Pirquet and Schick, is a very interesting one, and is the result of their study of the condition known as 'serum sickness'. They hold that the period of incubation

depends mainly on the production of antibodies in the system, and that the exciting cause of the illness does not itself produce intoxication until it is acted upon, after a certain interval, by these antagonistic substances. The interaction of the antigen, or provocative agent, and the antibody results in the formation of a secondary poison, to which Richet has given the name *apotoxin*, and which causes the symptoms of the disease. The production of the antibodies requires time, and this time coincides with the latent period of the illness. This theory, according to the view of von Pirquet, is applicable also to vaccinia, small-pox, and measles. Schick, however, has felt himself unable to reconcile it with the incubation stage of scarlet fever, which he regards as too variable in duration, and has contented himself with employing it to explain the occurrence of scarlatinal sequelæ. Whether the variability, or shortness, of the latent stage in any illness is sufficient reason for discarding the theory of von Pirquet and Schick, so far as that illness is concerned, is a question which, after all, they are best fitted to decide; but it seems a fair criticism to point out that the incubation period of serum sickness itself is, one might almost say, an exceptionally variable one, as a table on a later page (p. 442) will show. An explanation which is not applicable, according to its originators, to scarlet fever and diphtheria, has, it will be admitted, serious limitations, but we may grant freely that in the meantime it is as satisfying as any other.

TOXINS. The bacterial toxins are spoken of as being extra-cellular and intra-cellular. Those of the first group are given off into a fluid medium during the cultivation of the micro-organism, as in the case of diphtheria and tetanus. Other germs do not apparently render the medium toxic, but their dead bodies, when they have been killed by heat, exercise a marked toxic action, and these micro-organisms, therefore, are said to possess an intra-cellular toxin or endotoxin. This toxin may possibly be liberated by the micro-organisms during life within the human body, although *in vitro* such liberation does not occur. Or more probably the poison may be set free by the death and disintegration of the germs in the infected animal. Bacteria, again, in the process of growth, appear to produce poisons which are harmful to their own vitality and, in particular, ferments capable of dissolving the germs themselves and which are responsible, therefore, for the process of *auto-lysis* which, no doubt, sets free the intra-cellular toxins. Such autolysates have been made use of as vaccines for therapeutic purposes. Other toxins of a different nature, which have been termed aggressins, are apparently produced by certain bacteria. These, while perhaps not highly pathogenic in themselves, have the property of very much increasing the effectiveness of a dose of the bacterium employed and of transforming, in

fact, a non-lethal dose into a lethal one. It is believed that this property depends upon the paralysing action of the aggressins upon the phagocytic cells, and that resistance is weakened in consequence. According to another recent theory the toxins of bacteria are cleavage products derived from their proteid substance through the action of ferments present in the body of the infected individual. But, while too small an amount of such ferments might not be sufficient to cause toxic effects, they may be capable in too large an amount of destroying all the germs and breaking up the toxins themselves before they can do harm. This view may be reconciled with the explanation given of the occurrence of anaphylaxis under certain conditions, as it appears that all proteins, when acted upon by specific ferments, are capable of producing toxic effects. In their nature the toxins have been regarded as allied to albumoses, but it does not appear that much is known about them. The importance of isolating them is very great, as the preparation of antagognistic bodies, or antitoxins, depends upon their inoculation into animals. Such preparation is possible in the case of the extra-cellular toxins of diphtheria and tetanus, but in the meantime seems to be too much to expect in the case of the micro-organisms of which the toxins are intra-cellular. The toxins of different diseases exercise specific actions, some especially affecting certain tissues. Thus diphtheria toxin has a particularly deleterious effect on cardiac and nervous tissue.

IMMUNITY. The power of resistance of the individual to a particular infection is a variable quantity. It is in the first place in certain diseases influenced by the age of the person concerned ; thus as regards scarlet fever, as age advances the chances of contracting the disease, if exposed to it, are much diminished. On the other hand, should the disease be contracted, the power of successfully combating it may be weakened, as may be seen in the case of enteric fever against which advancing age, while affording some protection against infection, prejudices the recovery of the infected. Sex, though to a lesser extent, also exerts some influence in certain infections, but this, in some instances at least, would appear to depend more upon different habits of life than upon any fundamental sex distinction. It has long been recognized that, as apart from personal peculiarities, such conditions as fatigue, chill, or the exhaustion caused by an illness, may render an individual more liable to infection. Some persons may be exposed time after time to any given disease, and only succumb to it when their resistance is in some way weakened. Others, on the other hand, seem to be so susceptible that a very slight dose appears to be able to infect them, while it leaves other persons, equally exposed, quite unaffected. I remember a very curious instance of this undue susceptibility to infection. A boy

about seven years of age was admitted to the Edinburgh City Hospital suffering from measles. A week or two after his admission a patient was brought into the wards and, being found next day to be suffering from concurrent diphtheria, was promptly isolated. Of between fifty and sixty patients attended by the same staff of nurses this boy alone contracted diphtheria and, when free from measles infection, was transferred to a diphtheria ward. While there he alone of twenty-three patients contracted scarlet fever, introduced by a patient who afterwards commenced to desquamate. Removed to scarlet fever wards he was the only one of between seventy and eighty persons attended by the same nursing staff to contract chicken-pox, which had been unfortunately introduced by a child incubating that disease. In all the wards the great majority of the children exposed were unprotected by any previous attack against the diseases named, and all had, apparently, equal chances of contracting them. Particular families, again, may be especially susceptible to a particular disease, and individual members, attacked in different places and at different times, may suffer very severely from an infection which only affects normal persons very mildly.

Immunity may be either *natural* or *acquired*. There are some animals which it is practically impossible to infect with a given micro-organism. Thus rats and mice are not susceptible to diphtheria, and may be said to enjoy a natural immunity. It seems probable also that a certain power of resistance to infectious diseases is transmitted from generations of ancestors who have suffered from the diseases in question. It is difficult otherwise to account for the severity of certain infections when they appear for the first time, or after a long interval, in some isolated community, as was the case when the Fiji Islands were ravaged by measles. Certainly the worst cases of measles which I have seen have been in persons born in out-of-the-way districts of the Highlands or Islands, whose ancestors presumably were more or less protected from attacks of the disease by the conditions of natural isolation in which they lived. Immunity, on the other hand, may be acquired by passing through an attack of an infectious disease, this usually being sufficient to protect the individual against subsequent infection by the same micro-organism. Such immunity, however, is in some diseases of a very temporary character, and as regards erysipelas, influenza, and a common cold, the patient, so far from being protected, seems to be rendered even more susceptible to subsequent infections, a fact which may possibly be ultimately proved to depend upon anaphylactic phenomena. Immunity may also be acquired by the inoculation of non-virulent or dead cultures of the causative micro-organism, that is to say by vaccination, as is practised.

for instance, as a prophylactic measure against enteric fever. The injection of some antitoxic serums, as in the case of diphtheria, also confers a temporary immunity of short duration, and such immunity, depending upon the serum injected, and not upon the action of the individual, is termed *passive* to distinguish it from the *active* immunity acquired by vaccination or an actual attack of the disease.

How a patient recovers from an infectious disease and why, in many instances, the duration of the illness is, roughly speaking, the same in a given infection—e. g. typhus fever and lobar pneumonia—is only very imperfectly understood, and must still be regarded largely as a matter of theory. It is not now contended, as Pasteur suggested, that recovery depends upon the exhaustion of all existing material necessary for the growth of bacteria, or that, on the other hand, the micro-organisms are killed in the human body, as they sometimes are *in vitro*, by the gradual accumulation of their own excretory products. It would appear that the protection and recovery of the human organism is the result of an extremely complex process in which both the leucocytes and the fluids of the body take part. The leucocytes are usually increased in numbers as the result of infection, and this leucocytosis may be observed in the incubation period of some diseases. I have also noticed it in persons who were exposed to a disease but who ultimately did not contract it. Nevertheless it is well to remember that in some infections leucocytosis does not occur, as, for instance, uncomplicated enteric fever, in which the count may even be much below normal. *Phagocytosis*, however, no doubt plays an important part in protecting an individual against infection, and the leucocytes, according to the theory of Metchnikoff, contain digestive ferments which are set free by the breaking up of the cells. These ferments constitute the 'alexins', the substances which correspond to the 'complement' of Ehrlich. The power of the leucocytes to take up and destroy the infecting micro-organisms is now admitted to depend on the presence in the blood serum of certain substances which Wright has named 'opsonins', and which act upon the bacteria in such a way that they are readily digested by the white cells. The power of any given serum can be tested by mixing it with washed normal white corpuscles and with an emulsion of the appropriate bacteria, and the so-called opsonic index is calculated on the number of micro-organisms taken up by the cells. This recognition that the body fluids play some part in inducing phagocytic activity is particularly interesting as assisting to reconcile the phagocytic and humoral theories of immunity, neither of which, it may be remarked, is now regarded as completely satisfactory in itself. The humoral theory, advanced by Ehrlich, depends on the fact that blood serum of itself has

an inhibitory action on the growth of micro-organisms, and the principal substance in the serum responsible for this action has been termed 'complement', which corresponds to 'alexin', and is present in normal blood. Ehrlich holds that special atomic groups in the molecules of the body-cells have particular affinities for nutritive food-stuffs, which enter into combination with these 'side-chains' or receptors. On the other hand, bacterial products may also have special affinities for some of these atomic groups, and thus toxin may enter into combination with these groups, which are usually called 'amboceptors' or immune bodies. This may result in the death of the whole cell or only of the side-chain which is thrown off, leaving the cell to produce a new one in its place. The process of repair may go beyond what is absolutely necessary, and extra side-chains, capable of combining with the toxic molecules, are set free. In this way a substance which can combine with and neutralize toxin, an antitoxin in other words, may find its way into the blood, and on this theory the cells would respond appropriately to the foreign bodies capable of entering into combination with their atomic groups and thus render them innocuous. When gradually increasing doses of toxin are given to animals, this reaction of the cells is capable of setting free large quantities of antitoxin, and probably something similar occurs during the course of an infectious disease.

The body is also capable of elaborating other protective substances which act directly upon the bacteria themselves. Thus, if gradually increasing doses of bacteria are injected into an animal, in addition to the phagocytic power possessed by the cells, the serum becomes after a time 'bactericidal' and, by acting as it were as a solvent on cultures of bacteria, performs what is known as *bacteriolysis*. Such a bactericidal serum is not antitoxic, nor, on the other hand, is antitoxic serum bactericidal. Bacteriolysis requires both the 'immune body' which is produced in the tissues of the animal in process of immunization and also the 'alexin' which is present in normal blood serum. Another phenomenon which is associated with the protective process is *agglutination*. The blood of persons who have suffered from a disease, or of animals which have been inoculated with a particular micro-organism, acquires the power of agglutinating into masses or clumps the bacteria responsible for the infection in question. This reaction, which is stated to depend on the interaction of the agglutinin in the serum and of some substances in the bacterial cell, the agglutigen, is taken advantage of in the diagnosis of certain diseases, notably enteric fever. It is sufficiently specific for such a purpose, although so-called 'group reactions' may take place in the case of closely allied micro-organisms, such as paratyphoid and typhoid bacilli. Another reaction closely allied to agglutination

is that of the precipitins which are responsible for the precipitate formed in a bacterial filtrate when the appropriate anti-serum is added. The antibodies responsible for anaphylaxis have been identified by some observers with these precipitins. Other substances concerned in the protection of the body are hæmolysins, cytolytins, and so forth. Their relation to each other and to opsonins and agglutinins seems very imperfectly understood, and there is still much need for all the vast amount of work which has been done in the different branches of the subject being brought into co-ordination.

Natural immunity seems to be in most cases against infection and to depend on the power of destroying bacteria introduced into the tissues. It does not, however, necessarily imply that the animal is capable of resisting the toxins when injected separately.

It is more than probable that the various protective processes, briefly indicated above, may be to some extent assisted by the rise of temperature which is usually well marked from the onset of an infectious disease. We know, for instance, that outside the body the growth of most pathogenic organisms is much inhibited if the temperature of the incubator is allowed to rise even a few degrees above blood-heat. We also know that many of the changes which are found post mortem, and which used to be considered the damaging effects of elevated temperature, are in reality the result of toxæmia. They will be found in infected animals and human subjects, when there has been no pyrexia during life, and they have been proved to be absent in animals which have not been infected but in which the temperature has been artificially raised for a considerable period. It is again a fact that artificial reduction of temperature renders animals more susceptible to infection. The action of pyrexia, however, is still very obscure, and although clinically we may often welcome a good reaction to infection as evidenced by a high rise of temperature (see p. 17) we may freely admit that there is much to be said on both sides of the question.

Anaphylaxis. This term has been coined by Richet to express the condition of hypersensitiveness which has been found to follow the injection of certain albuminous substances. If an injection of horse-serum, for instance, be given to a guinea-pig and, an interval of at least twelve days having elapsed, a second injection, even of quite insignificant amount, is administered, the animal is taken seriously ill and may die in a few minutes with all the symptoms of shock. In this case it appears that the first injection has 'sensitized the animal to the particular form of albumin injected, and in the case of tox-albumins the result is the same even although a non-lethal dose is employed on both occasions and although the combined amount of the two doses is sub-toxic. There is no question, then, of any

cumulative action such as occurs with certain drugs. Further, this condition of hypersensitiveness is noted in tubercular patients and is evidenced by their capacity of reacting to tuberculin. It would appear then that the condition is one of exaggerated susceptibility to an albuminous substance, which may be natural to the individual or which may be induced by previous injections of the albumin in question.

The first injection of whatever albuminous substance is employed leads to the production of antibodies, or antiphylactic reaction bodies, the development of which requires a certain amount of time, the interval in fact which occurs before the establishment of the hypersensitive state. When the injection is repeated the albuminous substance, or *antigen*, by its interaction with its antibody produces the active poison called by Richet *apotoxin*, and this poison is responsible for the so-called anaphylactic shock. The serum of a sensitized animal, if injected into another animal, produces in the latter a sensitiveness resembling its own, that is to say, a condition of passive anaphylaxis is set up. The anaphylactic state has been proved to last in some cases for at least two years, but passive anaphylaxis is of short duration, usually disappearing in a few weeks. A point of great practical importance is that animals can be, as it were, 'vaccinated' against anaphylaxis by the administration of the antigen in considerable quantity before the twelfth day after the sensitizing dose, and that further, when already anaphylactic, they can be 'de-sensitized' by a very minute dose of the antigen itself. The bearing of this upon the employment of antitoxic serums and the relation of anaphylaxis to the so-called 'serum disease' will be discussed in another place (p. 437). It will be sufficient to mention here that the hypersensitive condition can be induced by the injection of almost any foreign protein, for instance bacteria or their toxins, egg albumin, milk, serum, animal poisons, plant albumins, and so forth, the reaction in each case being a specific one to the particular protein concerned. Idiosyncrasies to certain food-stuffs are also now regarded as anaphylactic phenomena. We have already seen (p. 6) how von Pirquet has attempted to explain the incubation period by this reaction, which he regards as, in reality, a reaction of immunity.

FEVER has been defined as 'a response in metabolism to the invasion of micro-organisms and a toxic disturbance of the regulation of temperature'. It is something more than a mere rise of temperature, which it is convenient to speak of as 'pyrexia'. The whole clinical picture of a fever may be observed in patients who manifest no pyrexia. Thus apyrexial enteric fever has not infrequently been reported, and charts illustrating it will be found on pages 293, 294. On the other hand, pyrexia, or, as

some would prefer to term it, 'hyperthermia', is seen in hysterical and nervous conditions which present none of the symptoms of true fever.

Nevertheless, we must regard a disturbance in the regulation of temperature as the cardinal sign of fever. The mean daily temperature in health is about 98.2 F., and the daily variation may be as much as two degrees. Muscular work may raise it considerably, and such a rise is strictly physiological and causes no ill effects. In health the temperature is perfectly regulated, and allows of perfect compensation for external heat or cold. In febrile conditions it is much more easily influenced by external causes, such as, for instance, a cold bath. We cannot, therefore, regard its regulation as being the same as in health, with the exception that it is 'set' at a higher level. Sometimes production of heat is much increased, and loss obviously diminished, as is the case in a rigor. A rise in temperature may be owing to the failure of the body to adjust the loss to the production. Should the loss be diminished, or relatively diminished, a rise must follow increased production; or, again, a rise may be due to the failure of the production to correspond with a diminished loss. Both factors are probably always concerned, and their want of correspondence is doubtless due to a toxic effect on the regulating mechanism. The *production* of heat takes place in the large glands and in the muscles. As regards *loss*, it occurs almost entirely from the skin, 70 per cent. being attributed to radiation and conduction, and 15 per cent. additional to evaporation of moisture. The remainder is lost by the respiratory tract, chiefly by evaporation, but partly by the loss in warming the inhaled air. Increased flow of blood to the skin, therefore, plays the chief part in the natural lowering of temperature. Sweating, as noticed at the crisis of some fevers, assists markedly in producing the fall.

As regards *metabolism*, the destructive phase of the process is exaggerated. There is increased respiratory exchange with a greater oxidation and discharge of carbon dioxide. The amount of urea excreted is also increased, and wasting is a very prominent feature of the febrile process. Moreover, owing to his loss of appetite and disordered digestion, the patient has to live upon his tissues, and the reserves of fat in the body are destroyed.

THE SYMPTOMS OF FEVER. In addition, then, to mere pyrexia, the fever patient, whatever be the infection, suffers from other symptoms, and these may now be briefly detailed. The pulse is accelerated, and usually so in a more or less definite ratio to the temperature elevation. This ratio may, however, be disturbed in certain fevers, as, for instance, in enteric and influenza, in which diseases the pulse, while moderately

quickened, often fails to attain the rate which the amount of pyrexia would lead us to expect. The rapidity of the respirations is also increased, as a rule proportionately to the temperature, but sometimes, as in diseases affecting the respiratory organs, such as pneumonia and measles, the acceleration is greater than the pyrexia warrants. Slight degrees of albuminuria may be present, but this again depends more upon the character of the toxin than on the height or prolongation of the temperature, for it is much more commonly observed in some diseases than in others. The urine is usually scanty and high coloured, the percentage of urea excreted is increased, and chlorides are usually much diminished in quantity, if not altogether absent. This latter point, however, has been regarded as due to the deficiency of chlorides in the usual fever diet of milk. Towards the end of a fever, and in the stage of defervescence, there may be a discharge of large quantities of pale-coloured urine. The digestive system practically always suffers, as is evidenced by a dry heavily-furred tongue, the diminution of the salivary secretion, marked loss of appetite, and imperfect gastric digestion. Constipation, also, is usually present. The patient complains much of thirst. The skin is hot and, in most fevers, dry. The derangement of the nervous system is shown by the headache, the insomnia, the delirium, and, no doubt, also by the frequent initial vomiting. Prominent among the subjective symptoms are feelings of chilliness, sensations of soreness or tenderness of the skin, and pains all over the body. Actual rigors may commence the process, but in many fevers they are only infrequently observed. Progressive wasting is characteristic of the more prolonged febrile diseases.

It is difficult to say how many of the above symptoms depend upon the elevated temperature. Probably very few, as they may be observed in such a condition as apyrexial typhoid, and, on the other hand, a healthy man, whose temperature may after strenuous exercise be raised as high as 101° F., presents none of them. It is more reasonable, then, to attribute them for the most part to the toxæmia, which is itself responsible for the pyrexia. It must, however, be frankly admitted that elevated temperature is, of itself, distressing to the patient, who is much more comfortable when it is falling than when it is rising or continuous. A fall of a degree, consequent on a cool sponging, will often cause a great feeling of comfort, and bring refreshing sleep.

Hyperpyrexia. It is unnecessary to follow the elaborate classification of Wunderlich according to the level attained by the temperature. It is purely artificial, and there is nothing to be gained by distinguishing between 'moderate' and 'considerable' temperature readings. The

practical point is, at what level does the pyrexia become injurious to the patient? What, in other words, constitutes hyperpyrexia? If we believe that, on the whole, the rise of temperature is a beneficial reaction, we shall judge more by the general condition of the patient than by the actual reading of the thermometer. It is unusual for a temperature of under 106° F. to be considered hyperpyretic, unless it shows no remission, or is unduly prolonged. When, however, that level is reached, it is well to be very careful to see that the temperature does not rise further, and the thermometer should be used at short intervals. Short of 106° , it may be said that those patients who show high temperature levels often make the best recoveries, and in children, particularly, unless other alarming symptoms are present, there is little need of interference. As to the highest level compatible with recovery, much depends upon the circumstances. I have seen several patients make good recoveries, whose temperature during a rigor exceeded 107.5° F. A man once under my care, suffering from some obscure fever picked up in the Mediterranean, had for over a week temperatures exceeding 109° , the elevation never lasting more than half an hour and being always accompanied by a violent rigor. For the rest of the twenty-four hours the temperature was normal or nearly so. I suspected a trick, but on several occasions the observation was controlled by three thermometers, one in each axilla and one in the rectum, with a doctor at each, and the patient was obviously desperately ill during the attack. On one or two days his temperature exceeded 110° , but he ultimately recovered.

THE STAGES OF FEVER. Following the period of incubation is the initial stage or period of *invasion* during which the temperature rises slowly or rapidly till the level, at which it will ultimately be maintained, is reached. This invasion stage differs considerably in the different fevers. The temperature may mount slowly and regularly as is often the case in enteric, it may be quite irregular or characterized by a definite remission, as is seen in measles, or it may rush up at once to its height, as is illustrated by many cases of scarlatina. The period, then, may last any time from a few hours to about a week. If the rise is abrupt it is often accompanied by definite rigors, and the patient is early prostrated. The invasion stage is followed by the fastigium or period of *advance*, which, in an eruptive fever, usually corresponds with the full development of the rash, and throughout which the temperature, with slight diurnal variations, remains at, roughly speaking, the same level. In duration this stage may be as short as twenty-four hours, or may, as in enteric, last for as long as from one to six weeks. The period of *defervescence* then succeeds, the tempera-

ture falling to normal, either rapidly or gradually. In the first instance it is said to occur by *crisis*, and the fall is accompanied by a marked and sudden amelioration of the symptoms. Sweating may be profuse in such cases. If the fall is more gradual, it is described as a *lysis*, the temperature slowly loosening, as it were, its hold upon the patient. Many examples of both forms of defervescence will be found illustrated by the charts throughout the volume. A lysis may be comparatively quick, or extremely protracted, and, on the other hand, the temperature of a patient, who shows all the general signs of recovery by crisis, may take two days to reach normal. After defervescence comes the period of *convalescence*, which in some eruptive fevers may coincide with the stage of desquamation.

As regards the character of the pyrexia, it is said to be 'continuous' if the range of daily variation is only slight, 'remittent' if the fall, usually noticed in the morning hours, exceeds a degree or a degree and a half, and 'intermittent' if accesses of fever are separated from each other by intervals of normal temperature. (See charts on pages 240, 295, 474, 552.)

MANAGEMENT AND TREATMENT OF FEVER. The main requisite is a large airy room. The fever patient does not catch cold, and there is no reason to avoid fresh air. On the contrary, a cool atmosphere is exceedingly soothing to him and assists in producing sleep, and, during the daytime, in diminishing restlessness. Hot stuffy rooms do positive harm. The patient must, of course, be kept in bed. The bedclothes should be light and, unless the temperature is excessive, care must be taken that they are sufficiently warm. On the other hand, a very easy way of reducing continued high fever is leaving the patient covered only by a single sheet, a method which has been dignified with the name of treatment by the 'ambient air'. Great care should be paid to the condition of the skin, which should be frequently sponged, and daily washed with soap and water. These precautions not only assist elimination by the skin, but also improve its general tone. The back should be rubbed with a little methylated spirit daily, this being particularly necessary when the fever is likely to be prolonged. A good nurse should always be procured.

Among the main principles of treatment laid down by our predecessors, that referring to the *reduction of temperature* used to stand out prominently. But, if we regard pyrexia as a beneficial reaction on the part of the human organism, our views on this point will have necessarily changed. It has already been suggested above that patients with high temperatures often seem to recover better than those in whom the reaction is less well marked. Holt found that in young children suffering from broncho-pneumonia, if

temperatures of over 105° are not included, the prognosis was progressively worse as the temperature was lower; that is to say, the mortality was considerably less in patients whose temperature exceeded 102° than in those in whom that level was never reached. Even the patients whose highest readings varied from 105° to 106° did better than those in whom they were under 102° . My own experience of broncho-pneumonia in measles and whooping-cough corroborates this view. The worst cases are those with the poorest temperature reactions. This is not to be taken as meaning that we would always sooner see a high temperature than a low one. On the contrary, it is obvious that a very mild infection will only be accompanied by a slight reaction. But it is none the less true that, given a patient who is obviously ill, a low temperature is often a bad sign. One of my chief troubles in hospital practice is that not infrequently the private family practitioner comes to see a patient, and goes home to inform the relatives that the temperature is 'nicely down'. We shall see, in diphtheria for instance, that the risks of the case usually begin just about the time that this 'desired' consummation is reached. The general public appears to have the firm conviction that, if the temperature is normal, all is well.

What we really should try to do is not to treat temperature as temperature, but to deal with its cause. That is to say, it should be rather our object to treat the toxæmia on which the pyrexia depends. This, of course, is not always possible, and, if hyperpyrexia is present, we have to do what we can to prevent the temperature remaining long at a dangerous level. And for this purpose hydrotherapeutic measures are undoubtedly the most effective. The temperature may often be satisfactorily controlled by the frequent use of sponges, not wrung out, but really dripping with cold or iced water. If this is not sufficient, the patient may be packed for a few minutes in a sheet wrung out of iced water and covered with a blanket, and such packs may be renewed at short intervals, as required, their effect usually being well marked. Or if the facilities for it are present, the cold bath may be employed, starting at a temperature of 65° or 70° , or, as some recommend, gradually cooled down from 90° , or even higher, according to the condition of the patient, and the fear of him suffering from shock. It is wise to rub the extremities briskly while the patient is in the bath. Much of the good which results from the use of these cold applications is the subsequent diuresis, which, by assisting the elimination of toxins, may be of permanent benefit to the patient. So far as the temperature is concerned, it often attains its previous level in an hour or two, and in really bad cases it is sometimes hardly affected at all. Other methods of applying

cold are the ice cap or ice coil to the head, and the 'ice cradle', which supports the bedclothes and to which small tin buckets of ice are attached. It is very difficult with the latter method to keep the extremities adequately warm. Instead of sponging, the patient may sometimes with advantage be rubbed down with blocks of ice. In my own practice I seldom find it necessary to go beyond this, or sponging with iced water.

In the eruptive fevers hyperpyrexia is often present in cases in which the rash is badly developed or of a bad colour. I am old-fashioned enough to believe that such patients will never do any good, unless the skin is made to act, and unless the natural efflorescence of the eruption is assisted. I do not, therefore, see much advantage in attempting to reduce the temperature by chilling the skin. If there is no reaction, and the circulation of such patients is often very poor, the last state is worse than the first, and after many years of treatment with cold water, I now much prefer hot. Hot sponges, hot packs, and fomentations wrung out of mustard and hot water, frequently renewed, appear to me in the long run to give better results. There is no objection, on the other hand, to applying an ice cap to the head, and an irrigation of the large intestine with cold water may, in emergency, have a marked effect in reducing temperature. Only too often, of course, the sudden ascent of the temperature to high levels is merely a symptom of approaching and inevitable death, and no treatment is of any avail.

It will be noticed that, so far, I have not thought it necessary to mention *antipyretic drugs*. The coal tar products, so often and, I think, so recklessly employed on the slightest pretext, certainly lower temperature, but they are, as a rule, of no real benefit to the patient. Occasionally good may be done by the action which they sometimes exert on the skin. To set off this, on the other hand, they have been proved to interfere with the excretion of toxins, and my predecessor, the late Dr. A. F. Wood, found that, when they were systematically employed in enteric fever, the duration of the disease, in patients so treated, averaged a week longer than in those for whom a purely expectant method of treatment was employed. The risk of collapse after their use must also be recollected. If any drug is to be used in hyperpyrexia, quinine is probably the safest, and for temperatures of over 107° there may be some justification for giving a dose of 15 grains, or even more. Personally, I have ceased to use it.

Besides reduction of temperature another great principle was laid down for us: *favour elimination*. This, I think, should be the motto to guide us in our treatment of infectious disease. The daily washing and sponging

of the skin will be of great assistance. Diuresis should be encouraged by the free administration of fluids, and for this purpose there is nothing better than cold water, the more the better. The condition of the bowels should be carefully looked to. An old writer on enteric fever remarked, 'Fuge purgantia tanquam pestem', but I should be inclined to say in all infectious diseases, 'avoid constipation like the plague'. There is no need for the patient to have more poisons to deal with than those of the disease itself. With a skin acting fairly well, a clean bowel, and increased diuresis, such a condition as the 'typhoid state' rapidly disappears, and restlessness, sleeplessness, and the like are seldom observed.

As regards the distressing *insomnia* of fevers, when present, it should be treated at once. It is not enough for the medical attendant to order a sleeping draught, and to leave it to chance whether it acts or not. The nurse must be given definite instructions as to when and how it is to be repeated, and the rule should be to see that a patient, who has been given a hypnotic, secures sleep. Otherwise he is left with one poison the more in his system, and no compensating advantage. I am accustomed to order a half-dose to be repeated every half-hour or hour, as the case may be, after the first, until what I regard as the maximum, compatible with safety, has been given, when I expect to be summoned at once to decide on further measures. Thus, if a dose of 20 grains each of chloral and bromide has been administered, 10-grain doses may be repeated twice at half-hour intervals, if the patient does not sleep. In some cases a small quantity of a different drug will have the desired effect. A patient may have received in the late afternoon 20 or 25 grains of sulphonal, and is not sleeping when the four hours which that particular drug usually requires have elapsed. Frequently, in such circumstances, a drachm or two of paraldehyde will have an instantaneous effect. Before, however, any hypnotics are employed every 'nursing' means to secure sleep should always be attempted. Tepid sponging, by lowering the temperature slightly, frequently induces sleep. A hot drink of milk, of beef-tea, or even of toddy, is often very useful. The cause of the sleeplessness must be considered. If it is headache, a very moderate dose of phenacetin or caffeine may be all that is required. If it is worry, few drugs are equal to a Dover's powder. In addition to the hypnotics mentioned above, bromidia, veronal, and chloralamid are all very useful on occasion.

It is also requisite, to use an old expression, to 'obviate the tendency to death' by appropriately supporting the circulation. We are now told that *alcohol* is not in reality a stimulant; but, provided that the pulse and general condition of the patient are improved by its use, we may thankfully

accept such improvement whether it is to be attributed to the stimulant or sedative properties of the drug. The latter are, indeed, most useful, and many a nervous and anxious patient will become brighter and calmer under the influence of quite small doses, such as, for instance, one drachm every four hours. In any case alcohol should be sparingly used and should be withdrawn if it does not appear to be effecting its purpose. That in many instances it improves the general circulation I have no doubt whatever, and its action on the skin capillaries makes it of great value in early cases of some of the exanthemata. As regards such drugs as *strophanthus* and *digitalis*, they will be usually found to be extremely disappointing in toxic and febrile conditions. *Strychnine*, on the other hand, often appears to benefit the circulation considerably, and, latterly I have had excellent results from the use of intramuscular injections of camphor in oil.

Open-air Treatment. Fever patients are nearly always much the better for treatment in the open air. It is of course necessary to protect them from rain, and by the use of hot bottles and extra coverings to secure their warmth. It is said that cold air has the effect of increasing the blood pressure, and there is no doubt that the pulse is often much improved. Patients treated in this manner sleep and eat better and their whole nervous tone is unquestionably improved. The method seems especially applicable to acute pulmonary conditions and to septicæmic cases such as patients suffering from septic scarlet fever and puerperal septicæmia. When the patient cannot be placed actually in the open air much may be done by widely opened windows in the ward itself, but it is remarkable how much better results can be obtained in the open air than in the most freely ventilated ward. It is unfortunate that few hospitals can do more than treat a few selected cases out of doors, and that the vagaries of our climate often make regular and prolonged treatment on these lines quite impossible.

SERUM AND VACCINE TREATMENT. In the case of those micro-organisms the toxin of which is extracellular, it is possible to prepare an *antitoxic* serum which may be made use of therapeutically. Such a serum is administered with the object of neutralizing the toxins of the disease, and this is effected by the combination of the toxic and antitoxic molecules which appear to have an affinity for each other. As diphtheria is the only disease discussed in this volume for which we have an antitoxic serum of established reputation, the reader is referred to the chapter on that subject for a general idea of the preparation and practical application of a serum of this type. An antitoxic serum has also the power of conferring a passive immunity of short duration. As regards intracellular toxins or endotoxins, doubts have been expressed by competent observers whether it is possible

to prepare the corresponding antitoxin, and in any case endotoxins do not appear to lead to the production of antitoxins with anything like the rapidity seen in the case of the extracellular toxins. Nevertheless encouraging results have been obtained by some workers in this field, and an anti-endotoxin for enteric fever is alluded to on a subsequent page (p. 364).

Many of the serums at present in use are *bactericidal* and for their preparation it is necessary to inject dead, and subsequently living, cultures into an animal with the result that protective substances are developed in its blood, and its serum can be employed therapeutically in the case of disease caused by the organism in question. Such a serum destroys the invading germs by bacteriolysis and may also depend for its effects on the opsonins and agglutinins which it contains. It is not, however, antitoxic, and it may possibly set free endotoxin in the process of breaking up the bacteria, although such a possibility may be disregarded clinically. Anti-streptococcal and antimeningococcal serums are of this bactericidal type.

The use of *convalescent serum* has been much recommended of late years. The great disadvantage of such a method of treatment is the difficulty in securing a suitable donor at the right moment. The intramuscular injection of 'whole blood', as practised by Zingher in scarlet fever, is so much simpler in technique than transfusion, and is so much more rapidly performed that we are likely to hear more of it (p. 147).

Vaccines. These are employed both for therapeutic and prophylactic purposes. A culture of the micro-organism required is either killed by heat or rendered avirulent, and is injected, usually subcutaneously, into the patient to stimulate his natural protective or resistive powers. So far it is as prophylactic agents that vaccines have been most successful, and those employed against enteric fever have been proved to be thoroughly reliable, an active immunity of considerable duration, though inferior to that conferred by an attack of the disease itself, being set up. Their therapeutic use, however, is still largely in the experimental stage, although in local infections, such as furunculosis, their employment has been attended by admirable results. Theoretically, when the local resistance has been lowered, much may be gained by stimulating the production of anti-bacterial substances in other parts of the body with a view of ultimately overwhelming the micro-organisms in the local focus of infection. The vaccines used may be either 'stock cultures', which have the advantage of being ready to hand when required, or 'autogenous', that is to say, prepared from germs obtained from the patient himself. Stock vaccines are often prepared from a number of different strains of the same organism and are then named 'polyvalent', such a vaccine being more likely to contain a certain amount

at least of the particular virus responsible for the patient's condition. Dosage is determined either by the weight in milligrams of a dried culture or by the estimated number of killed micro-organisms employed, and vaccines are standardized so as to contain so many millions or hundred millions per cubic centimetre.

Some workers prefer the use of *sensitized vaccines*. The emulsion of killed micro-organisms is gently shaken up with immune serum, which has been procured from an animal treated with increasing doses of the bacteria in question, and afterwards inactivated by heat. This mixture is then centrifuged and the residue of bacteria is washed several times in salt solution. Sensitization is said to hasten the lysis of the bacteria and to cause the earlier liberation of the chemical substances which promote the formation of antibodies. Besredka has also applied this process to emulsions of living micro-organisms.

Recently the *intravenous injection* of vaccines has been recommended. While this is often followed by a remarkable improvement in the patient's condition, there is reason to believe that the rigor and leucocytosis, which are usually observed and to which the benefit of the treatment may be not unreasonably attributed, are due more to the introduction into the blood-stream of a foreign protein than to any specific action of the germs themselves. It is indeed admitted that any kind of bacterium is as likely to be effective in typhoid fever, for example, as the bacillus typhosus itself. The improvement, then, is apparently secured by what has been called *protein shock therapy*. It is interesting to note that very similar results follow the intravenous injection of the colloidal metals.

There is no doubt that the modern tendency is to use vaccines somewhat recklessly and indiscriminately. When subcutaneous injection is adopted success cannot be expected unless the vaccine employed has been prepared from the same germ as is the cause of the disease, and it is advisable that that germ should have been isolated from the patient before vaccine treatment is undertaken. Dosage, again, is an extremely difficult matter, and, as things stand at present, it is not too much to say that the whole subject is in too experimental a stage for us to obtain reliable guidance on this point and on that of the interval which should be allowed between the doses. Too large a dose is liable to produce immediately after its injection a period of heightened susceptibility, the *negative phase*, and in any case it requires from 36 to 48 hours before free antibody formation occurs. The capacity of the production of antibacterial substances appears to be limited, and it is quite possible that more harm than good may result if the treatment is unduly pushed. It is satisfactory, however, to learn from competent

authorities that the risks of the negative phase have probably been somewhat exaggerated.

DIET IN FEVER. The increased metabolism, and consequent tissue waste, involved in the febrile process makes the consideration of the diet in acute infectious disease a matter of great importance. Except in the case of diphtheria, for which we have a really scientific remedy in antitoxic serum, we cannot hope by drugs or otherwise to limit the course of the disease. We can only stand by, and put the patient in the best possible condition for combating it. The primary necessity then is to *support the patient's strength*, which can only be effected by a suitable system of feeding and stimulation. If the fever is prolonged, this may be a matter of considerable difficulty, as there is no doubt that the gastric digestion is often much impaired by continued pyrexia and toxæmia, and salivary digestion is liable to be reduced to a minimum, the saliva being often much diminished and occasionally assuming an acid reaction. Pancreatic digestion also suffers, and in a prolonged fever it is chiefly upon intestinal digestion that the patient depends. Mastication, again, cannot be counted on in patients who may be much exhausted and often delirious. There is always, moreover, in the early stages of an acute fever, loss of appetite, and, only too often, disgust at food. Under such circumstances there is not much difficulty in concluding that the food given should be readily assimilable and, for the most part at least, fluid. We have seen above that it is highly desirable to favour the elimination of toxic substances, and that large quantities of diluent drinks, preferably cold water, are requisite during the fever.

If a patient is to profit by his food, it is very necessary that his desire for it should be, so far as possible, stimulated, and that he be put in the best possible condition for appreciating it. In this connexion no point is of more importance than *the toilet of the mouth*. A fever patient with dry baked tongue, and sordes on lips and teeth, will enjoy his food far better if his mouth is properly cleansed. Regular cleaning, moreover, helps to check the irregular fermentative processes which occur in the mouth, and which are liable to render the salivary secretion acid instead of alkaline. In severe cases the mouth and tongue should be carefully cleaned every four hours with a soft piece of clean rag, and afterwards anointed with some mild antiseptic ointment. A mixture of equal parts of boroglyceride and glycerine is suitable for this purpose, as is also the ointment used at the Edinburgh City Hospital, which consists of one drachm of boracic acid to the ounce of vaseline, flavoured with five drops of peppermint oil. An adequate supply of water also does much to keep the tongue moist and clean. The *serving of the food* is of importance. The glass and crockery

used should be scrupulously bright and clean. Neglect of this is quite sufficient to disgust a fastidious patient and renders him, in consequence, far more difficult to feed.

The food should be given in *measured quantities at measured intervals*, and the amount supplied at one time should be small. The rule should be 'little and often'. An interval of two hours between the feeds is a convenient time, but this may be in some cases more prolonged, the amounts given being slightly larger. As a general rule, the feeding should be continued throughout the night, but it will usually be sufficient to wake the patient at four-hour intervals. As a matter of fact, fever patients are, as a rule, so restless, and have their sleep so much broken, that a good nurse has plenty of opportunities of supplying them with food, without finding it necessary to wake them. If a feed has been missed, it is advisable not to increase the next one to such an extent that the loss is completely made up. It is extremely easy to overload the stomach, and most patients stand the occasional loss of a feed perfectly well. In special cases, when for instance a hypnotic has been given, or when the sleep has previously been insufficient, it would be madness to wake the patient in order to feed him, unless his colour becomes very bad or his extremities cold. Sleep in such a case probably conserves his energy better than food.

In ordinary cases, where the fever is not unduly prolonged, there is little or no advantage in giving more than fluid food. In a prolonged fever like enteric, or in the severe secondary fever of small-pox, this may have to be supplemented by soft solids, especially if the wasting is extreme, or if for any reason the patient enters upon the disease in a particularly debilitated condition. But in the shorter fevers such as measles, for instance, a fluid diet will be found perfectly adequate for the acute stage. The most satisfactory form of fluid feeding is unquestionably a *milk diet*, and, in children particularly, this need seldom be exceeded. Milk, containing as it does protein, fat, and carbohydrates, at first sight would appear the ideal form in which to administer fluid food, but, as will be seen in the chapter on enteric fever, theoretical objections to its exclusive use have been raised. If given properly, however, as described in that chapter, it is perfectly well digested by most patients. The milk may, under certain circumstances, be supplemented by *meat broths*, beef, mutton, veal, or chicken, and an occasional change in the basis of the broth does much to vary the monotony of the diet. The food value of these broths is no doubt very small, but they are usually much appreciated by the patient. The *different extracts of meat* and meat juices may also be employed with advantage, if the juice of fresh raw beef is not preferred. Another useful adjuvant to a milk

diet is *albumin water*. This may be prepared by shaking up the beaten white of a fresh egg in about 8 ounces of water to which a little crushed ice has been added. The whole may be flavoured with orange or lemon juice or with a small amount of sherry or brandy. Its employment may possibly in some degree provide compensation for the great loss of nitrogenous substances. I seldom, however, employ it myself except in prolonged cases. In such cases also, protein preparations of the class of somatose or plasmon may be suitably added to the diet, and in prolonged wasting conditions I have seen the greatest benefit follow the employment of sanatogen. Often a patient, who dislikes one of these foods, will quite readily tolerate another, and the medical attendant may also have his own preferences regarding them. I have always found Benger's food a most useful preparation, and employ it perhaps more frequently than any of the others named, though the cheapness of plasmon does much to commend it for hospital practice.

If, in spite of the addition of these various food substances to the milk, the patient appears inadequately nourished, cream or raw *eggs*, beaten up with milk and flavoured with brandy, may be added to the dietary. Bread and milk, well boiled, *arrowroot* and other starch preparations, milk chocolate, maltine, and *jellies* are also often admissible. As regards the latter, gelatine has a good reputation, as compensating tissue waste. The jelly may be prepared from calves' feet or from commercial gelatine. It may be flavoured either with wine or with fruit juices.

The above suggestions for a fever diet are, of course, entirely empirical. It is said that for a scientific diet an adult patient should be supplied with 3,000 calories. It appears to be useless to attempt to make up for nitrogenous waste by a great increase in the protein content of the diet, and that a supply of fats, and especially of carbohydrates, is more effective in maintaining the nitrogen balance. Coleman has found that a patient may actually gain weight during his fever on a liberal diet of milk, eggs, cream, butter, and lactose. Provided, however, the waste is not very excessive, it does not appear to do much harm to the patient and weight is readily regained in convalescence.

As regards *drinks*, pure cold water should always stand at the patient's bedside. If he is unconscious or delirious, it must be forced upon him. Aerated waters are, of course, largely used, and, without any enthusiasm for them, I must admit that a mildly alkaline water is probably sometimes of advantage. They tend occasionally, however, to the production of too much wind, and, when the digestion is feeble, they are better avoided. A little lemon or orange juice, in large quantities of water, sometimes

assists in allaying thirst, and in any case is grateful to the patient. But it is a question if we should endeavour to allay thirst, as it is by ingesting large quantities of fluid that the patient facilitates the elimination of toxins and waste products. Tea may be allowed in moderation in most fevers, and is best given with plenty of milk. Cocoa is tolerated if the digestion remains fairly good, and a little strong coffee, made with a large proportion of milk, is occasionally useful for patients who have a great dislike to milk given alone.

Diet in convalescence. With the return of the temperature to normal the first solids may be given, if the prolonged nature of the fever has not rendered their earlier use permissible. Sponge cake, or sponge biscuit, given with a cup of tea or a glass of milk, is a useful first addition to a fluid diet. Milk puddings, fish soups, meat soups flavoured with vegetable juices and thickened with rice or oatmeal, finely minced raw meat sandwiches, oysters, well-stewed fruit, and potatoes, well boiled and mashed with meat gravy or butter, are all suitable for the dietary of early convalescence. Thereafter, fish, whiting for choice, sweetbreads, and, in a few days, white meat such as chicken. From chicken the patient may progress to a chop, after which his digestion may be reasonably regarded as capable of dealing with any ordinary diet.

The above suggestions indicate very briefly the diet which may be usefully employed in pyrexial conditions. Each disease, however, has its own peculiarities, and may, from the nature of its pathology and its complications, demand special treatment. The dietary suitable for each will be found in its appropriate place, and it may be added that the principles of dieting enteric fever will be found useful in many other diseases.

DIAGNOSIS OF ERUPTIONS. It is hardly necessary to say anything about the general principles of diagnosis in the infectious diseases, but a few words, especially with reference to the diagnosis of eruptions, may not be out of place. When confronted by a doubtful rash the golden rule is to examine the patient from head to foot. Many mistakes in diagnosis depend upon the practitioner contenting himself with a casual glance at a face, chest, or arm. Such 'spot' methods are much to be deprecated, and can hardly fail to lead to disaster. There are few points in connexion with an eruption more important than its distribution on the body, and in some diseases, such as small-pox for instance, it may be said to be all-important. Again, a rash may be punctate on the chest, and coarsely papular, morbilliform, or even urticarial, in other situations, and diagnosis is naturally much influenced by such polymorphism. While the history of a patient's initial symptoms should always be investigated, as likely to

afford valuable indications, it must never be allowed to influence us too much, in comparison with the actual signs presented by the patient on examination. On the other hand, the presence or absence of constitutional symptoms, when a doubtful rash is under consideration, may occasionally decide the diagnosis for or against an eruptive fever in contradistinction to an adventitious rash depending upon drugs, serum, or intestinal conditions. When the presence of one of the exanthemata is suspected, and no rash is visible on the upper part of the body, it will be often found that the legs, if examined, will show the remains of a characteristic eruption. In most instances a rash appears last on the lower extremities, and, not infrequently, it is in that situation that it last fades. This forms another good reason for examining the whole body of a doubtful case.

PROPHYLAXIS. The first necessity, if control of infectious disease is to be effective, is the *notification* of the cases to the Medical Officer of Health. All infectious diseases are not compulsorily notifiable, and the lists adopted by different cities to some extent differ. Occasionally it may be found desirable to make notifiable for a specified period a disease which is not ordinarily reported. Thus during small-pox epidemics there is much to be said for the compulsory intimation of all cases of chicken-pox. The next consideration is the *isolation* of the patient. In the case of the more serious infections, as for instance small-pox, the isolation must be carried out in hospital. As regards less dangerous diseases, such as scarlatina, home isolation may be permitted if there is sufficient accommodation to carry it out satisfactorily. It is unusual for the non-notifiable diseases to be isolated, although in Edinburgh and Glasgow hospital accommodation is provided for measles and whooping-cough, and even chicken-pox and mumps are under certain circumstances admitted. *Quarantine*, or the detention of contacts in a reception house for the maximum incubation period, is very necessary in such a disease as typhus, and in any case, when serious infectious disease has broken out in the slums, it may be useful to remove all contacts from their homes, if only for a night, while cleaning and disinfecting processes are in progress. In the case of some diseases *preventive inoculation* is advisable. All small-pox contacts should, of course, be vaccinated, and the advisability of the use of vaccines in epidemics of influenza or enteric fever, or of prophylactic serum injections in outbreaks of diphtheria, should be considered.

Disinfection of the houses and of all fomites is, as a rule, to be advised. Few, indeed, would suggest that the disinfection of such fomites as the clothes worn by the patient or of his bed-linen could be safely dispensed with, except after those diseases, such as measles and rubella, in

which the virus is notoriously short-lived. The destruction or disinfection, moreover, of such articles as may have been contaminated by the secretions of the patient is obviously desirable, and this may be taken to apply to books and magazines, although the evidence of the transmission of disease by their means is by no means absolutely convincing. On the other hand, modern opinion is beginning to question whether the walls of rooms and such articles of furniture as chairs, desks, forms, and tables, harbour infection to any dangerous extent, and whether the substitution of ordinary thorough domestic cleaning for formal disinfection is not amply sufficient in the majority of cases. Thus Dr. Kerr, the principal School Medical Officer of the London County Council, does not consider the disinfection of school-rooms after outbreaks of infectious disease to be necessary. Some of our large fever hospitals have also ceased to disinfect their wards, with no evil results, and everything at present points to the gradual discarding of the expensive processes entailed by disinfection except so far as very serious diseases such as small-pox or anthrax are concerned. Chapin has carried out the interesting experiment of abandoning the 'terminal' disinfection of houses in which diphtheria and scarlet fever have been treated, and has compared the results with those of a previous period during which disinfection was in force. He has further compared the number of recurrences in these houses in Providence with figures relating to Baltimore, with the result that, so far as these two diseases are concerned, it may be said that the disinfection, or not, of the houses has practically no influence on the number of secondary cases. These are, after all, much more likely to be due to undetected carriers, that living source of infection which is so much more important than the walls and furnishings of the houses themselves.

It is true that the public attaches great importance to disinfection, and in this view it is supported by many public health officials. It is incumbent on us, therefore, to move cautiously in this matter, and I must confess to still disinfecting wards on occasion. But I have always felt that any good obtained was more from the thorough cleaning and subsequent free ventilation than from the particular disinfectant employed. Indeed for many years we depended on sulphur fumigation, a method now discredited as inefficient, and yet had every reason to be satisfied with the results. When, however, the disinfection of rooms is desirable, it may be effected by the use of either liquid or gaseous disinfectants. The application of the former in a finely divided spray is probably the most satisfactory, and formalin, a 40 per cent. aqueous solution of formic aldehyde, is the most suitable preparation for the purpose, as it is both economical and

efficient and neither blackens metals nor decolorizes clothing. It may be used in the strength of four ounces to the gallon. For small rooms the evaporation of formalin tablets in an Alformant lamp is a handy method of disinfection. In the case of the more serious diseases it is a wise precaution to strip the walls of paper. The German method of disinfection is to rub down the walls with bread and then wash the surfaces and the furniture with carbolic solution.

To disinfect clothing and similar textile articles steam should always be employed if possible. There are various types of steam disinfectors, but on the whole it may be said that a high-pressure steam apparatus disinfects more rapidly and efficiently than one through which steam circulates at a comparatively low pressure. It must be remembered that such articles as furs, boots and other leather goods, and books are destroyed by steam and can be exposed to formalin vapour or brushed with carbolic solution. The texture of blankets, also, is entirely spoiled by steam disinfection and any stains or grease marks on them become indelibly fixed. It is better, therefore, to trust to disinfecting solutions and carefully to avoid boiling them.

Recently attempts have been made to disinfect carriers and contacts by the use of the steam spray. Success has been claimed for this method in cerebro-spinal fever, and the system has also been applied in the case of measles contacts. The steam is conducted to a special disinfecting chamber on each side of which special jets are arranged along the wall at intervals of about five feet. In the room we have fitted up at the City Hospital the special jet used is that devised by Major Hine. A very fine spray is delivered and, by an attachment beneath the jet, disinfecting solution, chloramine T or zinc sulphate (1 per cent.) is sucked up from jars standing on a shelf below and vaporized. It is difficult to say how far this scheme is successful. It appears to be inefficacious in the case of diphtheria carriers, but may possibly shorten the detention of cerebro-spinal carriers. I am investigating its utility as regards measles and rubella contacts.

CHAPTER II

MEASLES

Nomenclature.	Complications: respiratory, ocular, ear inflammations, glands, enteritis, &c.
Ætiology: bacteriology, predisposing factors.	Pregnancy and Menstruation.
Dissemination and Infection.	Relapses and Second Attacks.
Period of Incubation.	Morbid Anatomy.
Period of Invasion: the catarrh, the remission, the enanthem.	The Blood in Measles.
Period of Advance and Eruption: the rash, the temperature.	Diagnosis: in prodromal stage, in eruptive stage, in convalescence.
Period of Defervescence: the crisis.	Prognosis and Mortality.
Period of Convalescence: the desquamation.	Treatment: management, diet, treatment of complications.
Types of Measles: mild types, severe types.	Prophylaxis: notification, school outbreaks, disinfection, and hospital isolation.

SYNONYMS—Morbilli, Rubeola. *French*, Rougeole. *German*, Masern.

NOMENCLATURE. It is of course unusual to hear this fever spoken of by any other name than that of 'measles'. The correct equivalent in Latin is 'morbilli'. But unfortunately the term 'rubeola' is also freely used to designate measles. This tends somewhat to confusion as the term is sometimes employed to signify German measles, and its equivalent in French, rubéole, is indeed the usual name in that country for the latter disease. It would be simpler if every one referred to measles as 'morbilli' and to German measles as 'rubella', and if the term rubeola were allowed to drop.

ÆTIOLOGY. It may be held as assumed that the cause of measles is a specific micro-organism. Although, however, a considerable amount of research has been devoted to this subject, we cannot at present accept as the real etiological factor any of the germs hitherto described by various observers. Some believe it to be a short bacillus as observed by Pielicke and Canon and also later by Barbier. A similar organism, a short slender bacillus, has been found in the blood during the stage of eruption by Borini, who was able to produce something resembling the disease by inoculating small animals. On the other hand, Lesage has described a micrococcus which he succeeded in isolating from the blood and nasal mucus of measles

patients, and which is also said to cause in rabbits a condition which resembles measles. Requisite proofs, however, of the specificity of these different organisms is not forthcoming; other observers, indeed, working on similar lines have failed to find them. While all are agreed that the infective agent certainly lies in the catarrhal discharges from the nose and eyes, many writers have claimed that the disease may be induced by the inoculation of the blood of a measles patient. To Hektoen belongs the credit of definitely demonstrating this fact. In 1905 he successfully reproduced the disease in two adults by inoculating them subcutaneously with blood taken from cases in the eruptive stage of measles. In 1910 Anderson and Goldberger were successful in producing fever and a typical measles eruption in Rhesus monkeys, which they inoculated with blood taken during the first eighteen hours of the eruptive stage in the human subject. Coryza, bronchitis, and in some instances broncho-pneumonia, also occurred. Similar results were obtained by the inoculation of nasal discharges. The incubation period was variable, but averaged from 6 to 8 days. The virus is apparently ultra-microscopic and passes through a Berkefeld filter. More recently Sellards and Wentworth have failed to produce the disease in monkeys.

Predisposing Factors. Measles is a disease which may occur in any *climate* and may apparently attack any race. Its geographical distribution may be said to be general. Females and males suffer in practically equal numbers, so no influence can be attributed to *sex*. The question of *age*, however, is more important. The disease is most common in the first five years of life, but can be contracted at any age. Infants of under six months appear to enjoy a certain degree of immunity, especially during the first three months of life, and it has been suggested that a natural immunity, inherited from a mother who has suffered herself from the disease, is effective for a limited time after birth. It has been stated also that whatever immunity does exist is not transmitted by the maternal milk, as measles is as likely to attack breast-fed as bottle-fed babies. It must be remembered, on the other hand, that very young infants enjoy a natural isolation which is not shared by older children, and that in any case, even at this early age, measles can hardly be said to be uncommon. The infection may even be taken *in utero*, instances having been reported of children born with the eruption fully developed when the mother was herself suffering from the fever. But we may doubt the influence of age in the light of the fact that when measles is introduced into a community, which has not been protected by previous epidemics, persons of all ages, including the oldest, are indiscriminately attacked. The prevalence of the

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A CASE OF MEASLES. Eruption fully developed on the face.

disease and its infectivity are such that, in ordinary circumstances, the average individual is exposed to it in early life and contracts it at the first exposure. Butler, in investigating the measles history of 14,000 persons in houses in which measles had occurred in connexion with the public elementary schools of Willesden, found that 97·3 per cent. of those over 15 years had had the disease, and it may be added that 90 per cent. of the deaths from measles in this country are of children in the first quinquennium of life. Of 12,362 patients treated at the Glasgow Fever Hospital, Brownlee reports 6,890, or more than half, were under five years of age. Of the remainder 4,146 were in the second five years of life, leaving only 1,326 who suffered at later periods. Of 800 infants in the first year 117 were under six months of age. In both Glasgow and Edinburgh it is noticed that an increase in the number of cases occurs between the ages of twenty and thirty years. This is explained by the fact that persons of both sexes, who have been brought up in distant villages under conditions of natural isolation, come into the cities at about the age of eighteen or later to seek employment. It is not long before they are exposed to infection, and they are as liable to contract it as the youngest children. At the Edinburgh City Hospital our female adult patients are for the most part girls from out of the way parts of the Highlands, who have come into service in town, and a large proportion of the men are Highland policemen or soldiers. In the well-known epidemics of the Faröe and Fiji islands it was noticed that all ages were equally attacked.

The disease, usually endemic in large cities, is apt to show epidemic prevalence, and this appears to some extent to be influenced by the *season*. Moore considers that a mean temperature of above 58·6° or below 42° is not favourable to its prevalence. Often two epidemic waves occur in the year, a higher one in December, January, and February, and one less well marked in May and June. In towns where the fever is endemic the epidemic prevalence often occurs only every second year,¹ but occasionally the wave occurs for several years in succession. It is possible that conditions which favour infection, such as the resuming of school attendance after the spring recess, have something to do with the increase of the disease so often noticed in May.

DISSEMINATION AND INFECTION. Measles is usually transmitted directly from person to person. The infective material lying, without

¹ Recent epidemiological researches by Brownlee go to show that in particular towns epidemics follow each other with some regularity after a definite interval. In Edinburgh, for instance, the intervals appear to be 98 weeks and 110 weeks, different organisms being presumably responsible for the outbreaks which occur at the different periods.

doubt, in the catarrhal discharges of the nose and eyes of the patient, may be disseminated by the act of sneezing or coughing. The spread of the illness is further favoured by the fact that the patient is infectious from the moment of his first symptom and may communicate the infection to others for several days before the nature of his complaint is recognized. While this preliminary catarrhal stage is the most infectious period of measles, the patient is also liable to infect others during the eruptive period. His infectivity, however, rapidly declines and probably ceases with the disappearance of the catarrh, which seldom outlasts the rash. I am aware that this view, which, it may be added, is also that of such authorities as Comby and Grancher, is not generally accepted, but I have never satisfied myself that I have seen infection communicated after the disappearance of the rash. Kerr, however, has reported an interesting case of a small girl who apparently infected several children a week after she was first isolated and an infant a fortnight later still, and, although there is always great difficulty in including less obvious causes of infection when measles is prevalent, we may admit that infectivity may be prolonged in exceptional cases, possibly by persistent catarrh. We may assume the infection to be usually of the droplet character and liable to be carried such a distance as it can be propelled in the act of coughing or sneezing. This distance has been computed by Armstrong at from 6 to 9 feet. The question as to whether a third person can carry the disease to others has been debated, but I think there is no doubt that the infection can be readily carried from one patient to another in the same building if the distance between them is not great. It is often so carried by nurses who are attending different patients in different rooms unless special precautions have been enjoined. Indeed it is only natural that a nurse, who has been perhaps sneezed upon by one patient, may infect another by handling him very shortly after. But the infection of measles is very short-lived, whether on the clothes of the attendant or on the *fomites* of the patient, and modern opinion doubts the necessity of disinfecting the latter. Another debated point is the possibility of convection by *air*. Armstrong's experience of the spread of the disease among the boys in a school chapel is strongly against a transmission of more than 9 feet, and although Grancher's experiments in the wards of a children's hospital were not free from accident he attributed the infections which did occur to carelessness on the part of the staff. Rundle at Liverpool has succeeded in nursing measles safely in a ward with other diseases, but it appears that his patients were in the eruptive stage, a period at which infectivity is usually not great. I am inclined to believe that a case in the infectious catarrhal stage could be treated without accident in a ward containing susceptible children, always provided the beds were from 12 to

15 feet apart and a special nurse provided, and that when measles breaks out in a ward it is carried by the staff rather than by the air. But I must admit I have not had the courage to put this view to the test.

There is no reason to believe that measles can be spread by milk or other articles of food. In the vast majority of cases the disease is no doubt first contracted at school and then imported to the younger children at home. It is by the control of school outbreaks that we must expect to influence the spread of the disease.

PERIOD OF INCUBATION. After the poison has been taken into the system, probably by inhalation, a considerable period elapses before the appearance of the symptoms. As to the exact length of this period there would appear to be a considerable difference of opinion. In this country it is usually held to vary between ten and fourteen days, but such extremes as five to eighteen days are also spoken of. A point of difficulty in determining the exact duration of the stage of incubation is the uncertainty as to when the infecting person first becomes infectious, and when the disease really commences in the person infected. Many observations seem to depend on the appearance of the rash as a fixed point. This is erroneous, as the period of invasion is most variable in its duration and may last as long as a week. In all probability the period from the moment of infection to the moment of the first symptom is from eight to twelve days, in most cases either nine or ten days. I have never seen a shorter incubation of which I could feel sure, although I must admit that, from the histories given by the relatives of some patients admitted to hospital, it would appear that the latent stage may occasionally last a day or two less. Herrman's careful observations go to show that the period lasts from seven to fourteen days, the great majority of the cases taking from nine to twelve days to develop. The rash in most instances appears in from eleven to fourteen days from the moment of exposure, but in some cases it may be delayed for a few days longer. For practical purposes fifteen days quarantine of an exposed person is usually sufficient, provided that a careful examination is made of the mucous membranes on the last day of his detention. Should these be normal, and no catarrhal symptoms or elevation of temperature be found to be present, he can be allowed to mix with other people. I have, however, seen four cases in which the incubation stage appeared to be as long as seventeen days. Such periods are so rare that they may be disregarded.

During the period of incubation the patient presents no symptoms. About the fourth or fifth day after infection, however, there is a progressive decrease in the body weight lasting usually until the commencement of the invasion stage. This is known as *Meunier's sign*, and its accuracy has been

confirmed by Armstrong, but it is not likely to be made much use of in practice. A leucocytosis has been described as occurring towards the end of this stage, and it is possible that, in hospitals, the systematic examination of the blood of exposed children about a week after the probable infection might be of value. Leucocytosis, however, is certainly not always present at this period.

PERIOD OF INVASION. Of all the stages of measles this is the most important and interesting—important because the patient is highly infectious from its commencement, interesting because the diagnosis is often most uncertain. It is characterized by three main features, catarrh, fever, and an enanthem on the mucous membranes. In addition, prodromal rashes of various kinds are occasionally met with. It varies very much in *duration*, the average being from three to four days. It very rarely lasts less than three and may be prolonged for as many as seven days. In addition to the catarrhal symptoms the patient suffers from some malaise, usually in proportion to the elevation of the temperature. Vomiting and shivering occur only occasionally, marked headache is not often complained of, and sore throat is rare. If a child, the patient as a rule ceases to take much interest in its toys and is less bright than usual. On the other hand, if the temperature is not high, he is usually able to run about, and seldom takes to his bed at once.

The *Catarrh* affects the eyes, nasal passages, larynx, and bronchial tubes. The eyes early become suffused, and after a day or two there is usually much lachrymation. The patient objects to light, and often does all he can to shield his eyes. Some cases, however, show little or nothing of this *photophobia*, and the eye symptoms may be limited to a slight congestion of the conjunctiva or even to undue redness of the caruncle at the inner canthus. Sneezing is usually a very early symptom, and almost invariably occurs sooner or later during this stage. An exposed person should always be isolated at the first sneeze, as nothing is more likely to disseminate infection. The nose runs freely, and the patient presents all the symptoms of a bad cold in the head. Hoarseness is a common symptom, giving evidence of a laryngeal catarrh, and occasionally laryngitis may become so marked that the case may be suspected to be one of laryngeal diphtheria. Bronchial catarrh, to a greater or less degree, is always present, and a short, harsh, irritable cough worries the patient. The catarrhal condition of the mucous membranes generally may often be evidenced by looseness of the bowels occasionally severe enough to deserve the name of diarrhœa.

The *Fever*, always present to a greater or less degree, varies very much in intensity and in its curve on the temperature chart. In spite of its great irregularity, I am inclined to believe that it approximates, as a rule,

to one of three types. Firstly, there is a type in which the temperature rises rapidly on the first day of the illness to a fairly high level, say to about 102° F., only to gradually decline with marked morning remissions till by the morning of the third or fourth day it is again normal. This tendency to return to the normal line, the *remission* of measles, is one of the most characteristic features of the fever (Fig. 1). In a second class the temperature is normal in the morning and elevated two or three degrees at

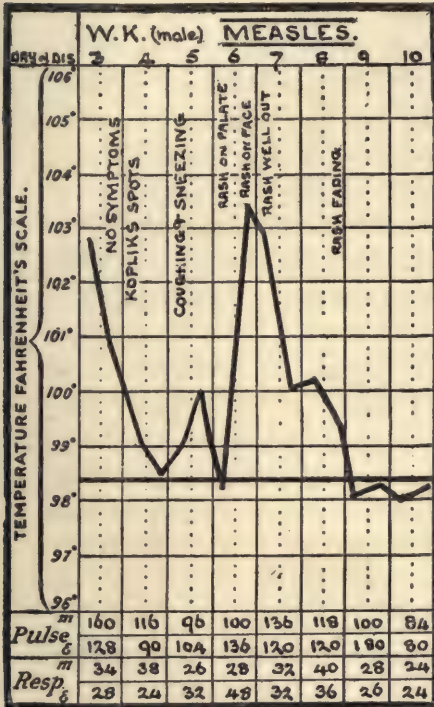


FIG. 1. A mild case of measles with well-marked initial fever, and somewhat prolonged remission. Rash not visible till evening of sixth day.

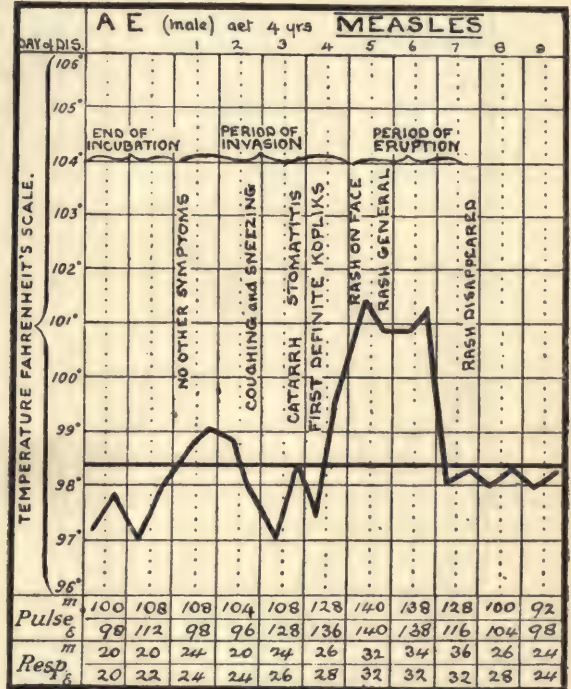


FIG. 2. A mild case of measles from the first day. Characterized by slight initial fever, a prolonged remission with subnormal temperature, and delay in the appearance of Koplik's spots.

night, assuming a remittent type. Similar to this are the cases where there is very slight fever, varying from normal to 99.5° F., but with less regular remission (Figs 2 and 4). Lastly, a small number of cases present a temperature which rises steadily from the moment of the first symptom till the rash makes its appearance (Fig. 3). In this type alone we do not find the otherwise characteristic remission. It may be noted that occasionally there is practically no pyrexia in the invasion stage, although sometimes the axillary temperature of a child, hitherto steadily subnormal, may give

useful warning by rising to the normal line (Fig. 5). I have also seen cases in which marked acceleration of the pulse, 130 to 150, was the only sign of disturbance apart from the catarrh and the enanthem. Even the catarrh may be almost entirely wanting in these afebrile cases, and it is often very much diminished during the remission of the ordinary fever.

The *enanthem* has been long recognized as one of the outstanding features of measles. The mucous membranes of the mouth are invariably

congested, and during the last day of the invasion period a blotchy rash may be seen on the palate. The recognition of this, however, is of little importance, as the patient has often been infectious for several days before it appears. A study of the buccal mucous membrane is of greater value. This invariably becomes somewhat swollen, and is less glistening and more dusky than normal. The suggestion presented is one of stomatitis, and there is often a mottled appearance. Sometimes thin pultaceous material may be seen as white or yellowish patches adhering to the inner surface of the cheeks and to the gums. The latter are usually slightly swollen and congested, and Tylecote considers this gingivitis of considerable diagnostic importance.

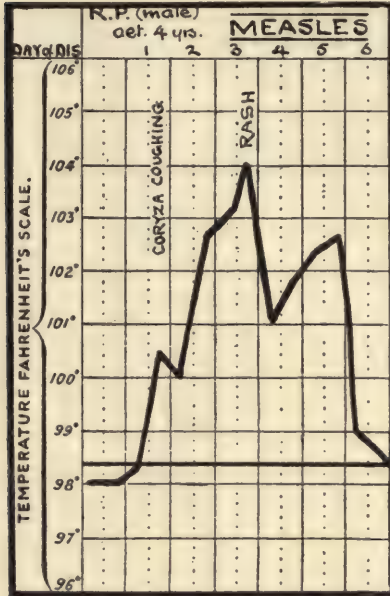


FIG. 3. Measles with an unusual prodromal temperature, showing no remission, but rising steadily till the rash appears.

More characteristic, and indeed quite pathognomonic, are the spots described by Koplik. These are minute bluish-white specks, usually surrounded with a bright red areola, which may appear on the buccal mucous membrane even on the first day of the period of invasion. The size of the whole spot, including the areola, does not exceed that of the head of a small pin, and is often much smaller. The spots have to be looked for in a good white light; indeed bright daylight is almost necessary for their certain recognition. At first few in number, they may be looked for at about the level of the first molar tooth, but as the invasion period progresses they become more numerous and cover the whole lining membrane of the cheeks, and may be seen inside the lips. They are more easy to recog-

nize before they become too numerous and too closely set together, as, when only few are present, they usually stand out distinctly with a definite areola upon a comparatively pale background. As they increase, the distinctness of the areola is lost, the subjacent membrane becoming darker and more congested, and by the time the eruption appears all that may be seen is myriads of pale specks on a very deep red surface. In an ordinary light the spots are often not seen at all, but the general congestion caused by their presence doubtless gives the appearance of stomatitis which was recognized long before the days of Koplik. It is worthy of note that the spots do not invade the palate. The rash which occurs there seems rather to be an early appearance of the same eruption which occurs later on the skin.

The importance of Koplik's spots will be realized when it is stated that they may be found even before the temperature has commenced to rise, and when the only other symptom is slight coryza. They are usually to be seen by the second day of the fever, but in a few instances their appearance may be delayed till just before the eruption shows itself. They are not found in conditions other than measles, and their value in diagnosis is therefore very great.

Prodromal Rashes occasionally occur during this period. Most frequently the rash is morbilliform in type, and leads to the belief that the real eruption is coming out early. It, however, completely disappears before the true rash, and is, moreover, badly developed and irregularly distributed. It is also much less papular in character, being hardly raised above the skin. Urticarial and scarlatiniform rashes also occasionally occur, and the latter may give some trouble in diagnosis. Prodromal rashes, if we except the first type described, have not been very common in my experience.

Herrman states that *leucopenia* is characteristic of the invasion stage and that it follows a leucocytosis which is present in the last days of the incubation period. The chart (Fig. 4) shows that this is not always the case, but when this sign is present it should be regarded as very suggestive.

PERIOD OF ADVANCE AND ERUPTION. This commences about the fourth day of the disease, and during this stage the symptoms of the patient are usually proportionate to the intensity of the eruption. The *catarrh* continues, but as a rule it is hardly so well marked, and the cough is less irritating than it was in the invasion period. The patient, however, is often sharply ill, and adults especially are extremely miserable and uncomfortable during the height of the eruption. It is rare for a patient to be able to keep his feet during the first two days of this stage, and his depression is often extreme. The *eruption* is usually first visible behind and

below the ears, and about the roots of the hair on the brow, but occasionally appears first on the trunk or limbs. The face, at first merely flushed, is soon invaded and the circumoral region is equally involved. The eruption spreads rapidly downwards over the upper part of the trunk and arms, and, within twenty-four hours of its appearance, the patient is covered from head to foot. Its duration is variable according to the severity of the case, but on an average it remains bright and well developed from twenty-

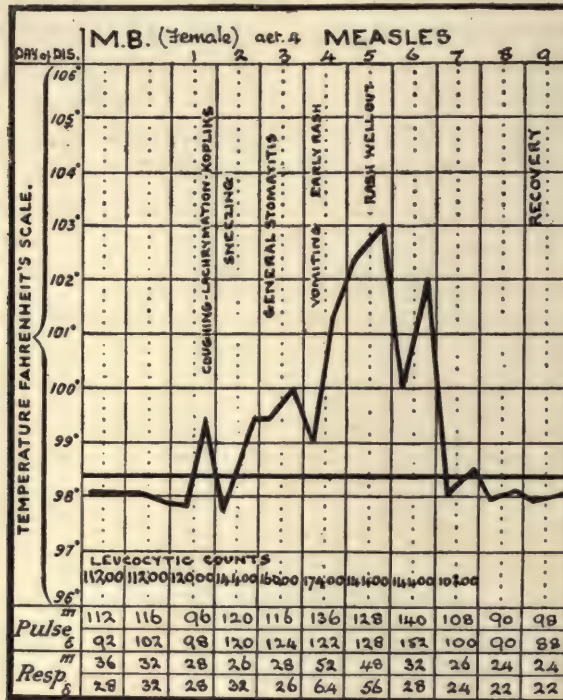


FIG. 4. Measles from the first day. Note that the leucocytosis during incubation is only slight, and that there is no leucopenia in the eruptive stage.

four to forty-eight hours from its first appearance. It then commences to fade, first on the face, then on the trunk and upper extremities, and last on the legs. It always, however, leaves more or less staining behind it, and this may be sufficiently well defined to give an accurate idea of its previous character and distribution. The eruption consists of papules, varying in colour from dusky red to pink, and well raised above the skin. These papules are grouped together irregularly in such a way that comparatively large areas of skin are altogether free from the eruption, and stand out as a dead white background to the rash. The grouped papules run together



THE ERUPTION OF MEASLES.

and coalesce into all sorts of irregularly shaped blotches or macules, many of which are often roughly crescentic in outline. The raised character of the eruption enables the papules to be readily appreciated by the finger gently drawn across the skin. They are soft to the touch, and it is usual to describe them as velvety. They disappear readily on pressure or on stretching the skin, unless indeed staining has begun or there has been hæmorrhage into them. This last not infrequently occurs, even if the case is not particularly severe, and is of little clinical significance, although the purple appearance of the eruption may look somewhat alarming.

While, as a rule, white areas of unaffected skin may be seen here and there all over the body, the eruption is occasionally extremely confluent. The back particularly, in a well-marked case, may present an absolutely uniform redness, complete coalescence of all the elements of the rash having occurred. The facies of the patient is highly characteristic. The discomfort which he suffers gives him a most woebegone appearance. The blotched face, bleary eyes, and puffy and swollen features together form a picture which, once seen, is easily recognized in future.

The staining left by the eruption, at first brownish-pink in colour, or dull purple if there has been hæmorrhage into the skin, gradually becomes yellowish as it fades. In some cases it may even resemble the dull mottling of the eruption of typhus fever. It often remains visible for several days, and I have seen it persist for nearly a fortnight from the first appearance of the rash.

The *temperature* during the stage of eruption is in the vast majority of cases very considerably raised. Readings of 104° and 105° F. are quite common, particularly in young children, and in the average case are usually higher than 103° (see Figs. 1, 3, 4). While the rash remains bright there is, as a rule, little or no remission. The brief summit of the measles temperature curve is comparatively flat. The *pulse* corresponds in its rise to that of the temperature. In young children a rate of 140 or more is frequently noticed (see Fig. 2), and need cause no particular anxiety. The *respirations*, as will be seen from the charts, are usually much increased in frequency. This is no doubt accounted for by the congested condition of the respiratory passages. Such symptoms as headache, delirium, and insomnia often occur during this period. The patient usually has a peculiar musty odour. This is pronounced enough for some nurses to assert that they are able to recognize the disease by their sense of smell, a power to which, I am afraid, I can personally make no claim.

PERIOD OF DEFERVESCENCE. The characteristic method of the decline of the measles temperature is undoubtedly by a slow *crisis*, lasting

from twelve to forty-eight hours before the normal is reached (see Figs. 1, 2, 3, 4). As the rash fades the temperature commences to fall. If this fall commences in the morning, there is often a slight swing up of the temperature in the evening, the following morning seeing the completion of the crisis. If, however, the fall commences later in the day a comparatively continuous fall of temperature is noticed on the chart. With the subsidence of the temperature there is a rapid amelioration of the symptoms, always provided no complications are present. The appetite and good spirits of the patient return rapidly, and he once more enjoys refreshing and unbroken sleep. There is no marked sweating during this critical change. The catarrhal symptoms by this time have usually subsided, the cough being the last to disappear.

PERIOD OF CONVALESCENCE. Provided there are no complications, this is rapid. The temperature at first is usually distinctly subnormal, and the pulse, not infrequently, may become markedly irregular. After the first couple of days the chief difficulty is to persuade the patient to be content to remain in bed. The staining of the eruption, as has been already noted, often persists into this stage and a slight but definite branny *desquamation* usually occurs. This is rarely prolonged for more than a fortnight from the first appearance of the rash.

TYPES OF MEASLES. These may be classed respectively as mild and severe. Two *mild types* of the disease have been described, *Morbilli sine Morbillis* and *Morbilli sine Catarrho*. Of these the first, I think, undoubtedly exists, but it is unquestionably very rare. A case which presents the classical symptoms of invasion, including coryza and Koplik's spots, may abort and no rash, worthy of the name, may be noticed, the temperature not rising appreciably after the prodromal fever. As to measles without catarrh, probably most of the cases described as such were in reality instances of rubella. On the other hand, it may be admitted that one occasionally meets with genuine cases of measles in which the catarrh is so trivial that it is not complained of by the patient or noticed by his friends. The most ordinary of the mild types of the fever is one in which all the classical symptoms are presented in a benign form, the fever is slight, the respirations little accelerated, the rash scanty and lasting but a short time. Complications, moreover, are rarely noticed. A true measles can undoubtedly run its course without the temperature exceeding 100° F. Goodall has even described cases in which no pyrexia at all was present. Such cases are very liable to be confused with rubella (Fig. 5).

Toxic types of the disease are also met with. Putting aside those cases which, from the first, assume an exceptional gravity owing to the early

appearance of respiratory complications, there are only two forms to consider. The first of these, the so-called *hæmorrhagic* measles, is extremely rare. I have never satisfied myself that I have seen a case. As described, it presents hæmorrhages scattered all over the skin in the form of purpuric spots and petechiæ, and the eruption is dark in colour. Hæmorrhage is also said to occur from the mucous membranes. It is more than probable that many of the cases described as 'black measles' by the older writers were in reality cases of hæmorrhagic small-pox, but as so great a clinician as Trousseau has described this variety it no doubt is occasionally met with. It must not, of course, be confused with that not uncommon form of measles, already mentioned, in which hæmorrhage occurs into the papules and the rash becomes purple. The latter may be comparatively mild in character, and the phenomenon would appear to depend rather on some peculiarity of the patient than on a special virulence of the infection.

The other severe type of measles has been variously called *Asthenic*, *Adynamic*, or *Ataxic* according as the symptoms of cardiac or nervous prostration predominate. It

covers all those cases of measles which succumb in the period of eruption, without obvious complications but from the intensity of the infection. No doubt, also, the powers of resistance of the patient have much to do with the production of this type, which is met with in tubercular, syphilitic, and cachectic children and, I am inclined to believe, also in persons of a naturally defective immunity. I have seen, for instance, at a time when the prevalent type of measles was not especially severe, four members of one family of seven succumb to an attack of the disease by which all were most seriously affected.

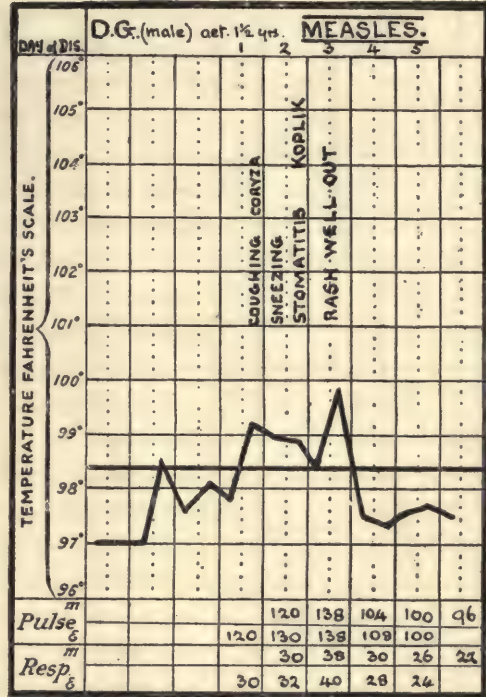


FIG. 5. A subacute, almost afebrile, case of measles. It is possible that the first symptom should be dated from the rise to normal, two days before the catarrh commenced.

Two of these cases died during the eruptive period, the other two very shortly after from complications. Now this particular family had just come into Edinburgh from the Fair Isle, and I think it extremely likely that, living in

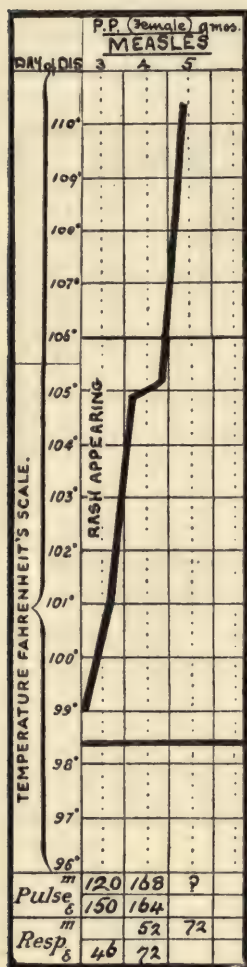


FIG. 6. A fatal uncomplicated case of measles in an infant. Rash badly developed.

conditions of such natural isolation, their ancestors had few chances of contracting measles and would transmit little or no protection to their descendants.

The main symptoms presented by a patient, who is unfortunate enough to contract measles of a severe type, are high fever (the temperature often reaching 105° or 106°), delirium, and marked prostration. The rash is sometimes exceedingly copious; in other cases its appearance seems to be delayed and it is badly developed. Even if it has come well out it loses its bright colour as the heart begins to fail, and becomes bluish in tint and less distinct. This is probably merely due to the weakness of the peripheral circulation. The pulse becomes increasingly rapid, the respirations shallow, and the patient dies in about three days from the appearance of the eruption, often in the typhoid state, and occasionally with hyperpyrexia. Fortunately such severe attacks of measles are comparatively rare (Fig. 6).

On the other hand, there is an asthenic type of the disease which is not uncommon in some epidemics, and is only seen in infants. During the prodromal period the patient does not seem particularly ill, but when the eruption appears there is a marked change for the worse. The eruption is usually well defined and of a satisfactory colour, but is not raised above the skin, and is very evanescent, lasting only a few hours, or, if persisting, becoming a pale violet in colour. The patient is extremely pale. There are no marked catarrhal or lung symptoms, the fever is as a rule moderate, but the pulse is unusually rapid. Treatment, with a view to keep-

ing out the rash, is not efficacious. Death occurs quite suddenly from heart failure usually before the crisis, but sometimes even two or three days after it with a subnormal temperature. I have seen infants, who had apparently passed safely through such an attack, die in their sleep without warning.

COMPLICATIONS. The great mortality caused by measles, however, is not due, strictly speaking, to the toxins of the disease itself, but rather to the complications which so frequently accompany it. The most important are, unquestionably, those of the respiratory system. Of these **respiratory complications** we may first mention *laryngitis*, which may declare itself early in the invasion period, may complicate the stage of eruption, or may even appear late in convalescence. Hoarseness is so common a feature in the prodromal stage of measles that some slight degree of laryngitis may be fairly regarded as a symptom rather than a complication of the disease. There may be nothing worse than some aphonia and a croupy cough. But, if to these symptoms dyspnoea is added, the condition must be taken seriously. It may be the result of a simple inflammation of the mucous membranes, it may depend on the presence of small ulcers in the neighbourhood of the vocal cords, or it may be diphtheritic in character. If it occurs in the prodromal stage it is usually, in my experience, simple in its nature. It may nevertheless present very grave symptoms. The patient is often cyanosed, the breathing laboured, and the pulse weak and rapid. It is quite common for such cases to be sent into a Fever Hospital in mistake for laryngeal diphtheria, the symptoms having become urgent, even two or three days before the appearance of the rash. Operation is occasionally necessary, but often with the efflorescence of the eruption the symptoms subside. Dyspnoea occurring during the eruptive period is more likely to depend on ulceration, occasionally followed by necrosis of the cartilages, or on the presence of a false membrane. Ulceration is probably more frequent in those cases in which broncho-pneumonia is also present, and which are more than ordinarily prostrated by the disease. If a false membrane is the cause of the difficulty, it may be due either to a true diphtheritic infection or to various pyogenic cocci. In either case the condition is extremely serious and operation in such circumstances is often unsuccessful. Lastly, laryngitis may occur in the convalescence of the disease after all acute symptoms have entirely subsided. It is safer to assume that croup occurring at this time is true diphtheria of the larynx, particularly if the patient is in hospital. But in a recent epidemic I have seen a very large number of convalescents develop a mild laryngitis with, for the most part, no dyspnoea, and satisfied myself, by repeated bacteriological examinations and by the uniformly benign character of the complication, that in these cases the diphtheria bacillus was not responsible for the croup. Previously my experience had been that croup *after* measles was always diphtheritic in its nature, and I still believe that in most epidemics it is so.

Bronchitis. As is the case with laryngitis, a certain amount of bronchial inflammation can be regarded more as a symptom than a complication of measles. But occasionally, after the disappearance of the eruption, the temperature continues to oscillate slightly above the normal line, the cough persists, and coarse râles are heard all over the chest. The patient presents none of the prostration which is so characteristic of broncho-pneumonia, and the respirations are only moderately accelerated, rarely exceeding forty, even in young children. The temperature seldom is higher than 101° F. and tends to be in the neighbourhood of the normal line in the mornings. This complication does not often last for more than a week after the disappearance of the rash and need not be regarded too seriously.

Of much more importance is the dreaded *broncho-pneumonia*, the complication which is responsible for the high mortality of measles. A great deal has been written with a view to making a distinction between it and acute capillary bronchitis on the one hand, and atelectasis on the other. Neither clinically nor pathologically are such distinctions usually possible. It is impossible to say when the inflammatory process involving the finer bronchi actually reaches the lung tissue. 'Capillary bronchitis and collapse of the lung', says Northrup, 'are but steps in the advance toward a broncho-pneumonia and cannot be separately considered.'

Broncho-pneumonia would appear to depend on a secondary infection by various cocci, the inflamed lining membrane of the air-passages doubtless forming a most excellent nidus for micro-organisms, and the depressed condition of the patient favouring infection. I have no doubt that the condition may be infectious from patient to patient, and the improved results which we have had in our new hospital, with its greater floor space and its more liberal cubic space per bed, go far to confirm this view. Under the more crowded conditions in our old buildings it was common to see the infection spread from bed to bed, whereas nowadays it is exceedingly rare for a patient to develop broncho-pneumonia after admission. Like laryngitis, the complication may appear in the prodromal stage, in the stage of eruption, or even late in convalescence. If it occurs early, it is often of the type we are accustomed to call acute capillary bronchitis, and is accompanied by noisy wheezing breathing, fine and coarse râles all over the chest, and often acute suffocative symptoms. Such patients may even die before the full development of the rash. Otherwise the worst symptoms of dyspnoea often disappear when the eruption is at its height, even if the pneumonic condition persists for some time into convalescence.

Most frequently, however, the first signs of commencing broncho-pneumonia are noticed during the eruptive period. The respiration is very

much accelerated, readings of sixty to eighty being often observed on the charts of children of under five years of age. Crepitations and small areas of dullness may or may not be found, auscultation being often difficult on account of the coarser râles which are almost invariable in measles at this period. It is wiser not to come to a definite diagnosis of bronchopneumonia until the rash has faded. If it is present, the temperature does not fall, or only falls slightly, with the disappearance of the eruption. The respirations remain as high as ever, and the pulse may vary from 140 to 170. The patient is prostrated and looks 'poisoned', there is more or less cyanosis, and the alæ of the nose expand with each inspiration. The cough is short and irritable and liable to be excited by feeding, but often is not very frequent. The amount of fever is variable, and, indeed, in some cases may be very slight. The gravity of the case is best gauged by the rapidity of pulse and respirations. An important sign is the fact that the ratio of respiration rate to pulse rate is usually altered, the respirations rising relatively more than the pulse. Often the lower intercostal spaces are sucked in on inspiration, and this sometimes is sufficient to suggest that obstruction is present in the upper passages. Occasionally our diagnosis of the condition must depend on the general appearance of the patient and the study of his chart (see Fig. 7). The examination of the chest is always difficult and sometimes disappointing. If the areas of inflammation are scattered over both lungs it is often difficult to hit upon a spot where fine crepitations, or bronchial breathing, can be heard, and, until some of the inflamed patches of lung coalesce, there may be little or no dullness. If dullness is found it is often due to atelectasis. In such a case the breath sounds are only faintly heard. If, on the other hand, comparatively loud bronchial breathing is recognized over a dull area, and fine crepitations are present, the diagnosis of pneumonia, already probably made by inspection of the patient and chart, is of course definitely established.

The symptoms presented by the patient are often much more severe than the mere condition of the lungs would appear to warrant. In addition to the defective aeration of the blood, there is undoubtedly also much toxæmia to contend with. The course of the illness is not unlike that of typhoid fever. Occasionally the inflammation may last for only a week or ten days. Much more frequently its duration is three or four weeks or even longer. The temperature may be irregular, occasionally remaining in the neighbourhood of the normal line for two or three days at a time, only to rise again as a fresh area of lung is invaded. During these intervals the pulse and respirations may also fall considerably, though seldom in proportion to the improvement in the temperature. Even when all symptoms

have apparently subsided and the patient appears convalescent, relapse may occur and the whole process be repeated.

It is not difficult to understand the exhaustion entailed by a complication in which the pulse may remain above 140 for a month, often, indeed, being much more rapid, and in which, for a similar period, the respirations may never have fallen below sixty, and have often exceeded eighty to the minute. If death occurs early, it is probably due to want

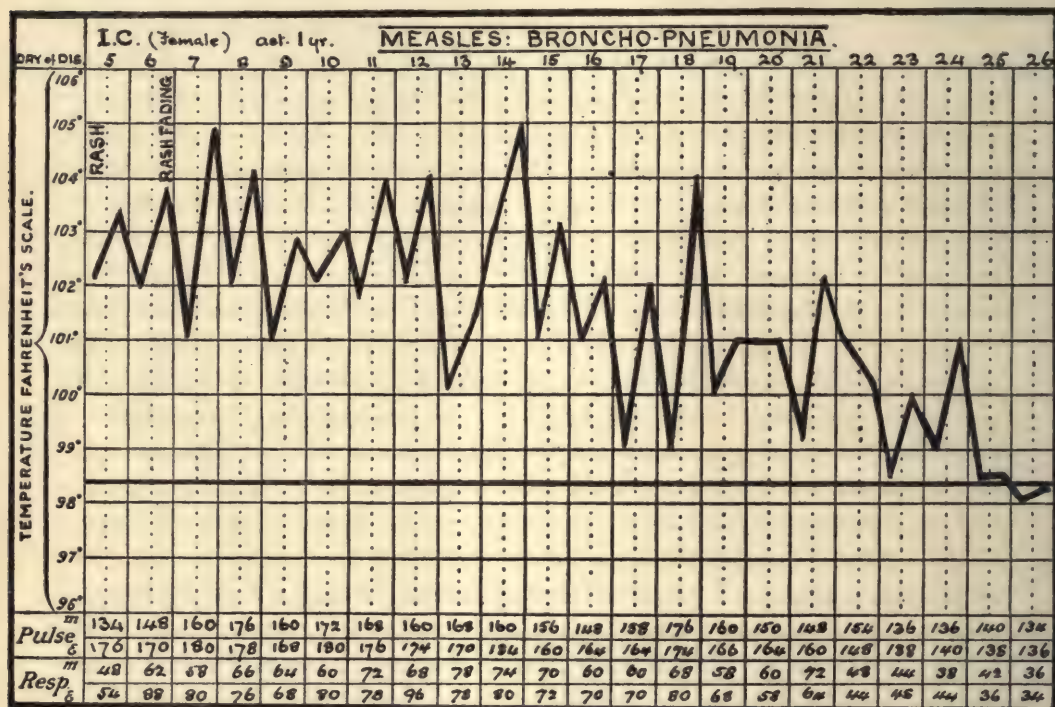


FIG. 7. A case of broncho-pneumonia, following measles, terminating in recovery. Note that the temperature, pulse, and respirations remained elevated on the sixth day, though the rash was beginning to fade.

of sufficient oxygenation of the blood. Cyanosis has, as a rule, been well marked in such cases. If, as is more often the case, death occurs after some three weeks of fever, it is more likely that gradual heart failure, from exhaustion and toxæmia, plays the most prominent part in its causation. In the prolonged cases pallor, cyanosis of the lips, and great tissue waste are usually the most prominent features. Death occurs in from one-third to a half of the patients affected.

Broncho-pneumonia is met with chiefly in children under five years of

age, and Comby estimates that a child below two years of age is about eight times more liable to contract it than a child of five. Out of 175 consecutive cases of my own, I find that 95 were less than two years of age, 29 of these being infants of under one year. Only 20 patients were between the ages of five and ten years, leaving 60 distributed among children of from two to five years. It is difficult to estimate with any accuracy how frequently the complication occurs. Hospital statistics are unreliable, as many of the measles patients admitted have been sent in because they are already suffering from broncho-pneumonia. At the Edinburgh City Hospital the percentage is from 10 to 12 of all cases treated. In private practice the incidence must be very much less. The cases are fairly equally divided between the sexes.

It is perhaps hardly necessary to class *lobar pneumonia* as a complication of measles. It certainly occurs occasionally, usually in older children or young adults, but very infrequently. The few cases which I have observed have been of a severe type and had a high rate of mortality. Several were followed by empyema.

As a French physician has well observed, measles is essentially a 'maladie tuberculisante'. *Tubercular conditions of the lungs* are common sequelæ, particularly if there has been a pneumonic complication. The condition of the whole respiratory tract favours tubercular infection, and any pre-existing lesion is apt to become acute. In a case of prolonged broncho-pneumonia, with much wasting and with fairly well localized physical signs, the presence of a tubercular complication should always be suspected. Occasionally a miliary tuberculosis may follow measles and meningitis may accompany the lung symptoms.

It is not without interest to note that a tubercular patient, who contracts measles, will fail to give a positive von Pirquet test in the eruptive period and for three or four days thereafter. It will be remarked that this stage of 'anergie', or failure to react, coincides with the period in which complications, such as broncho-pneumonia and diphtheria, often make their appearance, and also may explain the frequent extension of tubercular mischief during the measles process. On the other hand, the tendency to complications has been attributed by some writers to the leucopenia which is said to be characteristic of the eruptive stage.

Of considerable importance are **complications affecting the eyes**. From the commencement of the invasion period lachrymation and some slight degree of conjunctival inflammation have been present. The eye, therefore, has been in a condition which predisposes to infection by various micro-organisms. When ordinary cleanliness is neglected severe forms of inflamma-

tion occur very frequently, and may be serious enough to leave the vision permanently impaired. Simple blepharitis, purulent conjunctivitis, and keratitis with ulcer of the cornea are all common complications. Occasionally, but fortunately as a rule only in very ill-nourished and exhausted children, the ulcer of the cornea may perforate into the anterior chamber and a destructive panophthalmitis may result. More usually only small opacities remain as permanent evidence of the damage done by the disease. It is, of course, chiefly in hospital and in poor-class practice that these inflammations are met with, but it is well to remember that they may occur in any patient unless due attention is paid to the cleansing of the eyes. This ophthalmia is extremely contagious and if it appears in a hospital ward is very liable to be carried from bed to bed by careless nurses, who also may contract it themselves.

Important also, but not so easily avoided, are **inflammations of the ears**. Otitis media, sometimes accompanied by much pain, and usually followed by perforation of the drum and purulent discharge, is fairly common, occurring in from 2.6 to 8 per cent. of my cases in recent epidemics. Children under five years of age suffer in proportion at least twice as frequently as older patients. Mastoid disease may follow, but hardly so frequently, in my experience, as it does after scarlatinal otitis. On the other hand, we meet more persons who attribute their deafness to measles than to scarlatina. This may be due to the much greater number who suffer from measles, and to the fact that hospital isolation and systematic treatment of the otitis are not so frequently employed in that disease. In any case a considerable proportion of deaf-mutes appear to owe their disability to an attack of measles. Otitis usually does not appear till the stage of convalescence and may be accompanied by considerable pyrexia. In rare instances it may be followed by abscess of the brain or purulent meningitis.

A not unusual complication is **adenitis**, marked enlargement of the cervical lymphatic glands occurring in 2 or 3 per cent. of the patients. This condition, then, is not nearly so common as after scarlatina, and usually appears in debilitated or tubercular children. It is sometimes followed by suppuration of the glands. There is, as a rule, more or less irregular pyrexia, occasionally of a remittent character.

As has been stated previously, diarrhœa may occur in the prodromal stage. It is also not infrequently noticed during the eruptive period. It is seldom, however, serious unless it occurs in convalescence. At this stage a peculiar form of **enteritis** may retard the recovery of the patient, or may actually prove fatal. The stools consist chiefly of mucus and blood and may contain shreds of what looks like sloughs of mucous membrane. The motions

are frequent, and there is sometimes considerable pain in the abdomen. This form of diarrhoea may persist for weeks and is most likely to occur in patients suffering from a broncho-pneumonic or other exhausting complication. Pathologically it is probably a colitis, and appears to depend on some bacterial infection. It is apt to occur in small outbreaks, but is occasionally seen sporadically.

The above mentioned are the complications which are most usually met with in measles and to which that disease appears to predispose. There are many other conditions, however, which have been classed as complications, and which may be briefly mentioned. For instance, **nervous sequelæ** are frequently spoken of. Hemiplegia, disseminated myelitis, paraplegia, optic neuritis, muscular atrophy, chorea, tetany, and a form of neuritis resembling post-diphtheritic paralysis, have all been reported. Considering how universal measles is, it would be, indeed, strange if these conditions were not occasionally found either complicating or following it. I admit that I lose sight of my patients on an average about three weeks after the date of the rash, but still a large number remain under observation much longer. In a series of nearly 12,000 consecutive cases the only example of nervous complications which has come under my notice was one case of transverse myelitis in a young adult. I cannot, therefore, believe that measles plays an appreciable part in their causation. When meningitis occurs it is either tubercular or in connexion with otitis media. As in other acute diseases, convulsions are occasionally observed about the time of the appearance of the eruption.

Of more practical importance is *stomatitis*, which may be ulcerative and in rare instances is followed by *cancrum oris*, of which I have seen more cases after measles than after any other infectious disease. *Vulvitis* also, and very rarely *noma*, may be met with. *Nephritis* is extremely uncommon. I have only seen two typical cases in the convalescence of measles. Albuminuria may be present both in the febrile stage and afterwards, but is, as a rule, of little significance. Arthritis is infrequent and heart affections most uncommon.

The number of adults who contract measles is comparatively so small that little interest attaches to the relations of the infection to **pregnancy**. Abortion has occurred in a high proportion of the small number of pregnant women who have been under my care. I have not, however, noticed the tendency to septic infection which, it has been stated, exists in such cases. Authentic instances have been reported of the infant being infected through the placenta, and born in the catarrhal stage, or with the rash fully developed. Measles also appears to exercise a powerful influence on the occurrence of *menstruation*. I have for some years been interested in this question and

find that five out of six in a series of eighty adult females, admitted to hospital in the eruptive stage, were menstruating.

Relapse of measles is exceedingly rare. I have seen one case, however, in which a typical attack was followed seven or eight days later by a repetition of the disease with equally classical symptoms. Neither attack was in the least like rubella. The patient, a young female adult from the Highlands, made a good recovery. As regards *second attacks*, it is difficult to obtain satisfactory evidence. We often meet individuals who assure us that they have had measles two or even three times. One of these attacks has probably been rubella, and various forms of erythema may have been responsible for another. There is no reason why second attacks should not occasionally occur, as they undoubtedly do so in the other infectious diseases. But we may take it that they are very rare, and I have never satisfied myself that I have seen one. I incline to the view expressed by Herrman that a sign as definite and distinctive as Koplik's spots should have been identified in both illnesses before the reality of a second attack is admitted. It appears possible, however, that during a particular outbreak the disease may show a tendency to recur in the same individuals, and Dr. Sprent has sent me an interesting account of an epidemic in Hobart, Tasmania, during which second attacks, occurring from four to six weeks after the first, were extraordinarily frequent, the possibility of rubella being carefully excluded in every case.

Morbid Anatomy. It is so unusual for a measles patient to die, unless some complication exists, that the account of an autopsy is usually a description of a broncho-pneumonia, an ulcerative laryngitis, or some such condition. In those cases which succumb during the stage of eruption it is usual to find marked congestion of the mucous membrane of the respiratory tract, congestion of the lungs, and occasionally small hæmorrhages. The Peyer's patches of the small intestine are sometimes very prominent and much swollen. When broncho-pneumonia exists, its outstanding feature is the amount of pus which can be squeezed out of the darkly congested areas of lung.

The Blood in Measles. The condition of the blood in measles has recently received a considerable amount of attention. It is usually stated that during the last days of the incubation stage there is a well-marked leucocytosis which is also seen in the invasion period, whereas in the eruptive stage the white corpuscles are less numerous than normally. That there are exceptions to this rule may be seen by a study of the chart (Fig. 4). If it could be established, contrary to my own experience, that an uncomplicated case of measles always shows a definite leucopenia during the period of

eruption, the systematic examination of the blood might be of great use in distinguishing the fever from scarlatina and from serum eruptions in which leucocytosis is said to be the rule. But at present it would be unwise to lay too much stress on the value of the study of the blood-changes which are very liable to be disturbed by the presence of even slight complications. It may be noted that, during the incubation period, the increase in the number of the white corpuscles is due to a relative and absolute increase of the polynuclear cells (see p. 35).

The Urine in Measles. As has been seen above, albuminuria is occasionally met with in the febrile stage. The most interesting feature connected with the urine, however, is the practically invariable presence of the diazo reaction of Ehrlich (see p. 317). It may be well marked as long as the eruption remains bright upon the patient, but the most characteristic time to find it is when the temperature is just commencing to fall and the rash is beginning to show signs of fading.

DIAGNOSIS. This is chiefly a matter of difficulty in the **prodromal stage**. It is usually, however, only for patients known to have been exposed to measles that the medical man is called in early. In such cases the soundest rule is to isolate the patient at the first rise of temperature or at the first sneeze or other catarrhal symptom. If, in addition to one or both of these signs, there is the slightest suggestion of stomatitis, there is usually little or no doubt about the diagnosis. The presence of even a single Koplik's spot may be regarded as final and the patient may be safely isolated with other measles cases. The typical spots, however, may be late in their appearance, not becoming visible till the third or fourth day, by which time also there may be a distinct mottled rash on the palate. The temperature, unless the tendency to remission is well recognized, may prove rather a snare than an assistance. Too often, a patient, isolated for one or two days as a suspected measles, has been released from seclusion 'because his temperature is normal', and the appearance of a typical eruption twenty-four hours later has been a difficult phenomenon for the medical attendant to explain. A normal temperature, then, particularly in the morning, must on no account be held to contradict a diagnosis of measles, even if, as not infrequently happens, the catarrhal symptoms have subsided with the fever and the patient is apparently well. Looseness of the bowels, taken in conjunction with coryzal symptoms, should be regarded as a suggestive sign. The presence of erythematous rashes, often scarlatiniform, should in a suspected case rather strengthen than weaken the presumption that the patient is suffering from measles, always provided the classical symptoms of scarlatina are not present.

It will be seen, then, that, at this stage of the disease, we are reduced to saying that the only absolutely certain sign of measles is the presence of Koplik's spots. On the other hand, when we know a patient has been exposed, it would be foolish to wait for their appearance before isolating him. The necessity of looking for these spots in bright daylight has already been emphasized. Otherwise they are very easily missed. The only source of difficulty in recognizing them depends on the possible presence of minute food particles, bubbles of air, or small aphthous patches on the buccal mucous membrane. The latter spots are usually larger and are yellowish rather than white in colour. The areola, moreover, is seldom so well defined. It must be remembered that the absence of Koplik's spots does not exclude a diagnosis of measles.

The presence of laryngitis in the invasion period of measles should be an extra point in favour of an affirmative diagnosis, if the case is already suspicious. But, here, the difficulty of distinguishing the disease from *laryngeal diphtheria* may arise, especially if there is much dyspnoea. During a measles epidemic every case of laryngitis should be regarded as a possible measles, and the mouth carefully examined for Koplik's spots, stomatitis, or mottling of the palate. The presence of patches of false membrane on the fauces would of course establish a diagnosis of diphtheria, another good reason for always systematically examining the mouth and throat in such cases. If the mucous membranes are clean, even if no exudation is visible, the patient must be treated and isolated as diphtheria. But as, even then, it is difficult to make certain that it may not after all turn out to be measles, it would be unwise to place such a patient in a diphtheria ward, unless the Löffler bacillus has been obtained from the throat. When measles is epidemic, experience has taught me to isolate all cases of croup which present no definite faucial lesion or in which the culture is negative. Otherwise there is always a risk of introducing measles into a diphtheria ward.

In the **eruptive stage** the difficulty of diagnosis consists in the differentiation of the eruption from the other exanthemata, or from various skin conditions. To take these in detail, we first may have to distinguish the disease from *scarlatina*. This difficulty, as has been seen, may occur also in the prodromal stage, when the presence of a scarlatiniform rash may cause some trouble. But the absence of definite sore throat, rarely complained of in measles, and the presence of coryza and catarrhal symptoms, and possibly of Koplik's spots, should do much to prevent this error. In the eruptive period the marked involvement of the face, and particularly the region round the mouth, should usually exclude scarlatina. Even if

PLATE III.



MEASLES. While the rash is not very obvious on the face, the expression and eyes of the patient are fairly characteristic.

the patient has not been seen till the rash has become very confluent on the body and has for the most part left the face, it is usual to find sufficient staining left upon the circumoral region and upon the cheeks to make the diagnosis fairly clear. Still the measles eruption is sometimes absolutely confluent on the trunk and the most careful search may fail to find a typical measly appearance in that situation. In such a case it is wise to remember the excellent rule that an exanthem has not been properly examined unless the whole skin of the patient has been systematically inspected, and, as the eruption appears last on the legs, it will often be found there in the freshest and most typical condition, and may by its distinctly morbilliform character remove the last element of doubt. The absence of definite punctation, moreover, should cause suspicion that the case is not one of scarlatina, although it must be admitted that confluence is seen in scarlatina, as well as in measles. The history of the patient must of course be carefully studied. Sore throat, vomiting, headache, all point to scarlatina rather than to measles, while, on the other hand, marked photophobia, injected conjunctivæ, catarrhal symptoms, or laryngitis suggest the latter disease. The mucous membranes of the mouth are, as a rule, not particularly congested or oedematous in scarlatina, whereas in measles such a condition may be held to be the rule. It must be remembered that some cases of scarlatina show a very blotchy rash on the extremities (see Plate IX), and I have seen many such notified as measles. This is a grave error and suggests that the patient has not been properly examined, as usually the rash remains definitely punctate on the chest. Additional points to consider are the tongue, which, while it occasionally assumes the white strawberry appearance in measles, seldom desquamates in the characteristic scarlatinal manner, and the colour of the eruption, which is quite different, although it may be admitted that constant experience of both fevers is necessary before too much stress is laid upon it in diagnosis.

To distinguish a mild case of measles from *rubella* is often extremely difficult. The differential diagnosis will be found fully discussed in the chapter on the latter disease. It is enough to say here that the distinction will rest mainly on the well-marked prodromal catarrh which has usually preceded even the most trivial cases of measles, on the examination of the mucous membranes of the mouth, which are quite unaffected in rubella, and on the tendency of the rubella rash to become polymorphous in character, presenting different appearances in different parts of the body. The enlargement of the lymph glands, moreover, is much more obvious in rubella, especially when we remember that the more severe cases of measles, in which the glands may be considerably enlarged, are not the cases which

are likely to be confused with the less serious disease. The temperature, although always suggestive, is not a safe guide, as cases of measles may occasionally have little or no fever even during the period of eruption (see Fig. 5). Lastly, the diazo reaction, almost never to be found in rubella, might, if present, justify a diagnosis of measles.

As a rule there is little difficulty in distinguishing the disease from *small-pox*, but there are two periods in the latter disease at which a mistake is possible. Firstly, in the invasion period a morbilliform prodromal rash may occasionally present itself. This is distributed all over the body, as is the case in measles, the face being involved also (see Plate X). The rash, however, is not as a rule definitely raised above the skin, is not papular in fact. Still, I can imagine, if the patient by any chance should have a cold in the head at the same time, the diagnosis would be extremely difficult. However, under ordinary circumstances, the absence of catarrh, the severe prostration, and the presence of such symptoms as vomiting and pain in the back should help to indicate the real nature of the rash. Secondly, the true small-pox eruption, at its first appearance, may be mistaken for measles, which it occasionally resembles. Shottiness of the papules is not to be depended on. In varioloid the spots may be comparatively soft, and in measles, on the other hand, the papules on the brow often feel somewhat hard. In such cases I have found that the so-called 'Grisolle' sign, the disappearance of the feeling of hardness in measles when the skin is stretched, cannot be trusted. The history of the patient will be of much assistance, the early symptoms presented by the two fevers being fairly distinctive. If any doubt remains it is a good thing to take the temperature, and return to the case a few hours later, and note whether it has fallen or risen with the development of the eruption. The small-pox temperature falls with the outbreak of the eruption, often to normal, whereas that of measles nearly always rises. By this time, also, the tendency of the measles rash to become macular by the coalescence of the papules may give some assistance when the eruption is examined for a second time. In any case the difficulty is not likely to last more than twenty-four hours, and it is only the supreme importance of recognizing small-pox early which justifies the serious discussion of the differential diagnosis of the two fevers. Of course it is only when small-pox is epidemic that the question need be considered.

Typhus fever is so rarely met with that it is perhaps a little unnecessary to point out that its eruption has been mistaken for that of measles. I have also had cases of measles sent into hospital, notified as typhus. The error usually occurs in the case of children in whom a scattered eruption of

spots without hæmorrhage into the skin may remotely resemble a scanty measles rash. But in typhus the eruption never involves the face, and the absence of either rash or staining in that situation should remove all doubt, as indeed will the history of the previous symptoms of the patient, if carefully inquired into. Again, as Moore points out, usually the adults of a family are first affected by typhus, and, as the disease in adults is not very likely to be confused with measles, there is a probability that the exposure of the child to typhus infection can be ascertained. When measles is notified as typhus, it is nearly always a case which has been seen for the first time when the rash is faded and dusky, and severe broncho-pneumonia is present. Such a case may simulate the more serious disease very closely, but still the mistake should not frequently be made.

Syphilitic eruptions of a roseolar character have also been mistaken for measles. There should, however, be little difficulty in differentiating them. I have never, myself, seen a case in which this error has been made. It is said to occur most frequently when there is considerable secondary fever.

Rashes in infants due to the troubles of dentition and to intestinal disorders are also sometimes responsible for a wrong diagnosis. The temperature in these cases is usually normal and there is an absence of catarrh. They are likely to cause most confusion when it is known that the patient has been exposed to measles. In older persons rashes of a very similar nature may be due to various food substances. I have seen on several occasions a very fair imitation of a measles rash follow the eating of mussels. As a rule, however, such rashes are apt to be multiform in character, and, if the whole body is examined, the apparent resemblance becomes much less.

Serum rashes are not always easy to distinguish from measles, although the difficulty does not arise so frequently as it does in connexion with their differentiation from scarlatina. A morbilliform antitoxin rash may resemble that of measles very closely, but the absence of prodromal catarrh and of Koplik's spots should prevent much hesitation before coming to a correct conclusion. Moreover, even the most typically morbilliform serum rashes have usually a multiform character on some part or other of the body, and have the peculiarity, so often noticed in these eruptions, of disappearing rapidly and reappearing again after a few hours.

Drug rashes must also be considered. The one of which I have had most experience is that caused by copaiba or similar balsams. I have had several such cases sent into hospital as measles. The distribution of the rash is sometimes similar, but the colour is usually quite different, and catarrhal and buccal symptoms are, of course, wanting. The tempera-

ture, however, is occasionally elevated. Turpentine, chloral, and antipyrin are all said to occasionally cause rashes which may be mistaken for measles, but, in my experience, these eruptions are much more likely to be confused with scarlatina.

Septic rashes sometimes have a superficial resemblance to the measles eruption. A case of septic scarlatina, for instance, which has lasted some weeks, and in which the poisoning is profound, may present a blotchy eruption on the face which morphologically is morbilliform. Such rashes, however, are very irregularly distributed on the body and tend to show great patches of angry redness in the neighbourhood of the joints. There may be, of course, discharge from the nose, but the typical catarrhal symptoms of measles are absent. Once the possibility of pyogenic cocci causing such rashes is understood, mistakes are not likely to happen.

Occasionally it may be necessary to attempt to diagnose measles in the **stage of convalescence**. That is to say, the medical attendant may be called in after the rash has disappeared. Diagnosis in such cases must depend largely on the history of the invasion symptoms suffered by the patient. It will be often difficult to obtain a satisfactory description of the rash, but the average mother can usually say whether there were distinct blotches on the face or not. If this has been the case it is extremely improbable that the rash has been that of scarlatina. The staining left by the measles eruption is usually recognizable for a day or two at the least after the eruption itself has disappeared, and its mottled character and faint brownish colour often make the diagnosis quite easy. If there has been any history of sore throat, and the tongue approximates in appearance to the 'red strawberry' type, it is safest to watch for characteristic scarlatinal desquamation, with which the branny, furfuraceous powdering of measles is not likely to be confused. Till this point is settled the patient should be isolated, and his seclusion should last at least three weeks, or a week longer than is necessary when measles has been definitely diagnosed.

As regards the **diagnosis of complications** little need be said. During the eruptive stage it is exceedingly difficult to make certain of the exact nature of the chest condition, as the bronchial catarrh which exists in all cases is often noisy enough to make the appreciation of pneumonic sounds by the stethoscope almost impossible. Uncomplicated cases, again, if there is much pyrexia, may have great rapidity of respiration, and, if no dull areas are discovered, it is generally safer to postpone a definite diagnosis till the eruption commences to fade. If, in spite of the disappearance of the exanthem, the temperature and respirations

remain up, the patient is almost certainly suffering from broncho-pneumonia. A rise of temperature in convalescence suggests adenitis or otitis, unless a heightened rate of respiration and some coughing point rather to a late pneumonic complication.

PROGNOSIS. It is too often the custom, especially among the general public, to speak of measles as if it was a most trivial ailment. It may be freely admitted that, in good-class practice and under favourable circumstances, the disease may often be most benign in character, but it should never be forgotten that the percentage case mortality may be very considerable. And, apart from this, measles may leave behind it disablements of all sorts,—opacities of the cornea and impaired vision, sometimes total blindness, not infrequently deafness, partial or complete, and lastly, various lung conditions such as emphysema or, what is more serious still, tubercular disease. While, then, we need not as a rule be too anxious about healthy children living under good conditions, our prognosis regarding weakly children, the population of the slums, and, broadly speaking, hospital patients, must be to some extent guarded.

During the last nine years of the compulsory notification of measles in Edinburgh, there were 38,283 cases with a mortality rate of 3.25 per cent. This is certainly an understatement of the true death-rate, as many of the cases intimated were probably rubella, a disease which never terminates fatally. We may, therefore, assume that the percentage case mortality was not less than 4, a figure which is sufficiently high to draw attention to the fact that measles is a really serious disease. Hospital death-rates are considerably higher, the class of patients admitted coming largely from the poorest districts. Of 4,310 patients admitted to the Edinburgh City Hospital during the period named, no less than 6.75 per cent. died. This relatively high mortality is also shown by the Glasgow Fever Hospital figures, a percentage mortality of 9.1 being noted in 12,362 cases. Such figures may be greatly increased under certain conditions, especially when the majority of the patients are very young. Thus, of 1,575 cases which occurred in the Hospice des Enfants Assistés at Paris, in the five years ending in 1886, no less than 46.22 per cent. succumbed, and of 2,585, treated at the Hôpital des Enfants Malades at about the same time, the death-rate was 40 per cent. We may conclude, however, that overcrowding, insufficient ventilation, outbreaks of diphtheria, and not improbably bad nursing, must have had much to do with a mortality so excessive.

Prognosis, in fact, must depend largely upon the conditions under which the patient is going to be treated. *Overcrowding*, either in the home

or the hospital, will always influence it unfavourably. The children of the poor, nursed in small and often dark rooms, cannot be expected to have a low rate of mortality. In hospital again, where the aggregation of large numbers of patients increases the risk of infective complications, free ventilation and ample floor space are essential if good results are to be expected. If wards are allowed to become overcrowded, broncho-pneumonia, which may be broadly said to determine the mortality rate, will spread from patient to patient. Another most important point is the question of *age*. During the first half-year of life the mortality is not quite so high as in the succeeding six months, and the death-rate reaches its maximum in the second year. Thereafter it progressively falls and, after the fifth year is passed, becomes relatively trifling. Adults, indeed, do not, under ordinary conditions, usually die of measles, their comparative freedom from complications being much in their favour. But soldiers, in crowded camps or billets, occasionally show a high fatality rate. The Highland Territorial Division in an epidemic at Bedford, as shown in a chart prepared by Colonel Dewar, lost 60 men and in one of its battalions over 14 per cent. of the patients succumbed. It is true that the Highlander usually takes measles badly, and I have noticed a similar susceptibility to its virus in Australasian troops. The death-rate in measles does not rise after adolescence, as it does in scarlet fever, but in aged people it is apt to be very high.

If there is any *pre-existing disease*, such as tubercle or syphilis, the chances of recovery are much diminished. In my experience a very large proportion of measles deaths take place in children with some constitutional taint. Such conditions are often noticed in patients who succumb in, or shortly after, the eruptive period, and it is only natural that the presence of tubercle should make recovery from broncho-pneumonia almost hopeless. Defective nourishment, insufficient clothing, and want of care during the invasion period all increase the liability to complications, and it is upon complications that the mortality from the disease for the most part depends.

During the *eruptive period*, as long as the rash remains brilliant in colour, it is as a rule unnecessary to be anxious about the level of the temperature, provided it does not exceed 106° F. But should high pyrexia persist and the rash at the same time lose its colour and show signs of disappearing, the outlook is very serious. Such a fading of the rash often means a failing circulation, and should always cause alarm. Severe head symptoms of a meningitic character are a very bad sign, as is also a small rapid running pulse.

The actual presence of definite *complications* influences unfavourably

the prognosis. Laryngitis should be regarded seriously if there is any dyspnoea. Even if not diphtheritic in nature, it sometimes turns the scale against a weakly child, and it is often accompanied by extensive bronchitis of a suffocative nature. If, however, the latter is not present, the dyspnoea may disappear with the efflorescence of the eruption. The great cause of death in measles, broncho-pneumonia, has a mortality varying from about 20 to 80 per cent. according to the age of the patient, children of under two years having an extremely poor chance of recovery. In this complication the dangers are more or less proportionate to the rate of the respirations and pulse. If both remain constantly very frequent, with no remissions, the outlook is much worse than when some rest is given to the patient by occasional days of more easy breathing. I have never found the course of the temperature of much value in prognosis in broncho-pneumonia. Often the worst cases are, so far as the pyrexia is concerned, subacute, whereas a high temperature sometimes seems to point to a good reaction rather than to any extension of the inflammation (see Introduction, p. 18). A very pale complexion and cyanotic lips denote a bad case, as does also recession of the lower intercostal spaces. It is well to remember, on the other hand, that young children, however ill they may look, sometimes make most marvellous recoveries, and if they continue to take their nourishment fairly well and secure an adequate amount of sleep, there is always a ray of hope.

Should diphtheria complicate measles, the prognosis is always grave. It has long been recognized that the two diseases, should they run concurrently, are both unfavourably influenced. As, occasionally, it is only the measles which has been diagnosed, severe symptoms of croup, or purulent discharge from the nostrils may be the first signs that diphtheria has complicated the case from the onset. And, even in these days of serum treatment, the mortality of cases injected after three or four days is relatively high and, when measles is also present, may be excessive. Again, it is notorious that tracheotomy, or intubation, performed in such cases gives extremely poor results. If, however, diphtheria merely supervenes during the convalescent period, and its appearance is recognized at once, the prognosis is quite good if there is no delay in giving antitoxin. In hospital, particularly, the death-rate from this cause may be reduced to a minimum, whereas in the days before serum treatment was the rule such cases were usually fatal. Curiously enough, measles, occurring in the convalescence of diphtheria, is in my experience usually benign.

TREATMENT. As there is no specific remedy which can cut short the disease, our treatment is limited to putting the patient in as favourable

a condition as possible to resist it, to preventing, so far as may be, the occurrence of complications, and to treating these complications as they arise. In the first place, rest in bed, from the moment the fever is suspected, is essential. Much harm is done to patients by allowing them to run about when in the prodromal stage. The room should be large, light, and well ventilated. Owing to the photophobia which is so frequently present, the bed should be so placed that the light does not strike directly on the eyes of the patient, but, on the other hand, it is unwise to nurse any infectious disease in a darkened room. At the Edinburgh City Hospital the measles wards are painted a restful green, and this, to some extent, modifies the effect of the great amount of light admitted. There is no need to be afraid of plenty of fresh air; indeed, the more free the ventilation the less chance of broncho-pneumonia. Nevertheless, draughts, playing directly upon the patient, are to be avoided.

The strength of the patient must be maintained by a suitable *diet*. On the few occasions on which we have the opportunity of treating the disease in the prodromal stage, if the fever is trivial, soft solids may be permitted, always provided there is no diarrhoea. During the eruptive stage and the high fever which accompanies it, the diet may be, with advantage, limited to milk alone. Children, who are the chief sufferers from measles, seldom require more. In adults, if the bowels are not unduly loose, beef-tea, chicken jelly, or eggs beaten up in milk may also be allowed. Water should be supplied freely to patients of all ages, and this may be flavoured with the juice of oranges or lemons, if desired. When once the temperature has fallen, more nourishment may be supplied, first milk puddings and other soft solids, afterwards fish and solid food. In children it is wise to increase the diet cautiously, always remembering the possibility of enteritis being set up by an unsuitable diet. For this reason I prefer to keep children on milk puddings, bread and butter or jam, and white fish, for ten days after the crisis. With adults more liberality is quite safe. Meat soups, stewed fruit, chicken, and, after a week's normal temperature, butcher's-meat may all be allowed. Strong broths and thick vegetable soups occasionally cause outbreaks of diarrhoea in children, and for that reason should not be given to any patient less than ten years of age. But a moderate amount of beef-tea, or chicken-tea, may be permitted.

Care in the regulation of the diet, then, may lessen the tendency to enteritis. As regards the other complications, we have already seen that free ventilation is, particularly in hospitals, a safeguard to some extent against outbreaks of broncho-pneumonia. Other precautions against this dangerous condition, which may be of some value, are the protection of

the chest by a light cotton-wool jacket in those children who have a tendency to bronchitis, and regular rubbing with stimulating oils. The preparation which I am in the habit of using is a mixture of the oils of cajuput, eucalyptus, and olive in equal parts. A very important feature of treatment is the *toilet of the eyes*, which should be cleansed night and morning with boracic lotion. Needless to say, sponges are not to be used in hospital for this purpose, but clean cotton-wool swabs, which should be destroyed after use. Should ophthalmia break out in a ward, I have found that occasionally painting the eyes of the unaffected children with a weak solution, 5 grs. to ʒi, of silver nitrate is efficacious in preventing the spread of infection.

During the acute stage of the disease it may be occasionally necessary to treat symptoms. *Cough* is often irritating and persistent, especially at night. A cough mixture containing a little tinct. camph. co. made up with tincture of squills, or syrup of tolu, and chloroform water is sometimes useful, or ipecacuanha wine or carbonate of ammonia may be given. Patients often do well with the paregoric alone. The *temperature* should not be interfered with, unless it reaches such levels as 106° F. In such a case cool sponges or a bath at about 98° F. may be employed. The frequent use of tepid sponges in cases in which the temperature exceeds 104° F. is comforting to the patient and does not disturb the course of the fever to any extent. All patients should, of course, be sponged for the sake of comfort and cleanliness both night and morning throughout the illness. Ice applied to the head is soothing when excitement and delirium are present, but the temperature must be carefully watched and any too great depression of it avoided. If *insomnia* is present, hot drinks, cool sponges, and treatment of the cough, which is so often responsible for it, are the best therapeutic measures. Occasionally a hypnotic—for children I prefer small doses of bromide of sodium or paraldehyde given by the rectum—will be required. Should the *eruption* fail to develop satisfactorily, hot baths, packing with blankets and hot bottles, or fomentations wrung out of mustard and hot water will be usually effective. Similar treatment is indicated for *convulsions*. Should *vomiting* be persistent, the milk should be peptonized or iced, and hot applications may be made to the epigastrium. *Diarrhœa* is sometimes troublesome in the eruptive period, and may be best dealt with by boiling, or adding limewater to, the milk, by irrigation of the large intestine with hot water, and by the use of chalk mixture, astringents, and, in very severe cases, small doses of opium or an opium and starch enema.

If complications are present, they must be treated appropriately. For

laryngitis a steam tent will be necessary, if there is any dyspnoea. Adults often find much relief from ordinary steam inhalations. Hot fomentations round the neck are also very useful. It is well in cases of extreme respiratory difficulty in the prodromal stage to postpone surgical interference as long as possible, as the worst symptoms are often alleviated by the efflorescence of the rash. Should the *laryngitis* be diphtheritic, antitoxin must be given at once. In croup occurring during convalescence it is wise to give serum first and diagnose the cause of the complication afterwards. The acute suffocative form of *broncho-pneumonia* will require active treatment. Much as I dislike poultices, I think that in this condition they may be of great service, and one of linseed and mustard between the shoulder-blades or on the front of the chest sometimes gives considerable relief. When the more acutely bronchitic symptoms subside, a cotton-wool jacket is an essential, and the chest should be well rubbed with the three oils. A moist atmosphere, if not actually a steam tent, is desirable in this particular form of the lung complication. In treating the ordinary type of *broncho-pneumonia* we must remember that we have to deal with a febrile condition which may last for several weeks. The diet, then, should be for the most part fluid, but must also be a little more liberal than that for the eruptive stage. In addition to the milk we may give albumin water, various proprietary foods such as Benger's, plasmon, sanatogen, &c., chicken jelly, raw meat juice, or the different meat extracts. Egg-flip, white wine whey, and wine jellies may also be permitted. Stimulants are often necessary. The treatment of *broncho-pneumonia* under open-air conditions may be depended upon to give satisfactory results. My own patients, unless it is actually raining, spend the day on the ward balconies both winter and summer, and at night are placed in a special room, the atmosphere of which is kept, so far as possible, similar to that out of doors. I consider that this method of treatment has four advantages. Firstly, the patients lose much of that restlessness which is so characteristic of *broncho-pneumonia* and obtain much more sleep. Secondly, they are often eager for their food, and one of the greatest difficulties in treating the condition is thus abolished. Thirdly, they have much less chance of acquiring tuberculosis, and lastly, being kept out of the main ward, they are not likely to infect other children. I am now content to depend upon open air and suitable diet for the treatment of these cases, and, beyond seeing that the chest is adequately protected, seldom order anything further. A little ammonium carbonate will occasionally help the cough, and in very cyanotic cases I have sometimes imagined that the use of leeches was of some service. Cold affusions to the chest stimulate the respiration and no

doubt may help the return of the air to collapsed areas. I only use them, however, in very bad cases with much dullness in the chest. Strychnine and strophanthus are both of value if the patient shows much exhaustion. I have recently tried the mixed vaccine known as phylacogen in a small number of cases of broncho-pneumonia, but with only moderate success.

When *conjunctivitis* has declared itself the eyes must be frequently bathed with boracic or weak corrosive lotion, and it is wise to paint with silver nitrate, 5 or 10 grs. to ζ i, once daily or every second day. This, if employed early, will often check the progress of the inflammation, or, if preferred, protargol, 2 per cent., can be used for this purpose. The ointment of the yellow oxide of mercury is the best preparation to use for ulcer of the cornea. A little atropine is a useful addition to this ointment, should photophobia be present, and a shade should be placed over both eyes. If *otorrhœa* occurs, the ear must be syringed frequently, every four hours if necessary, with peroxide of hydrogen or boracic acid solution. *Adenitis* may be treated by fomentations of 1–80 carbolic acid, frequently renewed, or the neck may be merely wrapped in cotton-wool. Should there be supuration, the glands must, of course, be opened. In all the above conditions the patient is the better for systematic tonic treatment with such drugs as syrup of the iodide of iron or Easton's syrup, and cod-liver oil may be given freely. *Enteritis* is often most resistant to treatment. The diet should be limited to milk, preferably zymized, with lime-water, and with perhaps the addition of raw meat juice, or bovine, and to small quantities of Benger's food. The bowel should be irrigated two or three times daily with hot saline solution. A little grey powder, or small doses of calomel or perchloride of mercury, may also be found useful. Occasionally a starch enema with a few drops of laudanum will be necessary. Any other complications must be dealt with on ordinary lines.

PROPHYLAXIS. The great infectivity of measles, and the fact that it is most infectious before it can be easily diagnosed, make its efficient prophylaxis a matter of extreme difficulty. On the other hand, it will always remain a matter of the greatest importance when the high mortality of the disease is considered. *Notification* has not had the results which it has given for the other infectious fevers. This is natural enough, as the average case disseminates infection for several days before it can be notified. Those cities which adopted compulsory notification, Edinburgh and Aberdeen for example, found that it did not justify the great expense entailed, and after a trial discontinued the system. But the Local Government Board in its recent decision¹ to make notification compulsory in England was undoubtedly

¹ This order has been already rescinded.

right. While fully recognizing the great calls upon modern municipalities, I cannot but feel that there is little chance of progress if the Medical Officer of Health has not complete knowledge of all the infectious disease in his district. In Edinburgh, a system of *school notification*, rendered comparatively easy by the recent arrangements for medical inspection, has done something to solve the problem, and the health authorities have succeeded in isolating at least as many patients as in the days of notification. It has long been recognized that the aggregation of large numbers of small children in schools is chiefly responsible for measles epidemics. Once these school outbreaks are properly held in check, we may confidently expect a great diminution in the general mortality from the disease, as there will be much less likelihood of the very young children at home becoming infected. *Closure of schools* has not been found a very satisfactory method and is productive of an enormous waste of school time. Still, in certain outbreaks it has proved effective. Thus Mostyn reports that after closing seven schools in South Shields for three weeks, cases only occurred in three of them when they were reopened.

To secure a really efficient method of protection it will be necessary for the Medical Inspectors of Schools to acquire an accurate knowledge of the history of the school-children. Eberstaller at Graz keeps a list of all the children and the diseases which they take, and, if an outbreak occurs, does not find it necessary to keep children, who have had measles, away from school. He can always furnish the authorities with a certificate that a given individual has already suffered from measles, and such a pupil continues to attend school. It should never be assumed, if a certificate is not forthcoming, that children of over twelve years of age may safely be held to have had measles, and as control becomes more perfect, it is obvious that such an assumption will become more and more unsafe. It may be taken for granted, however, for practical purposes, that a pupil who has once had the disease will not take it again. We have already seen that second attacks of measles are extremely uncommon. Again, assuming a case of measles has occurred in a school, it would be very unwise to trust to the daily examination of the mucous membranes of a class, or to the taking of temperatures and the exclusion of children with coryza. Even in the most skilled hands there are too great chances of error for such a method to be successful. The best procedure is to exclude all children who have not had measles from the ninth to the fourteenth day after the occurrence of the first case, limiting this exclusion to children of the same class and allowing those in other classes to continue their work, unless, of course, they are related to the first case. Eberstaller gives an instance of the working of this method. A boy in a school at Graz was sent home coughing on April 22. The case turning out to be one of measles,

his class was closed from May 1 to 6 inclusive. During these six days no less than sixteen of his classmates developed measles, all in their own homes, but apart from this there were no more cases. The amount of school time saved in this manner must be very considerable. It is necessary to send a printed notice to the parents of the children affected, warning them of their exposure and suggesting that they should be isolated at the first sneeze. The point, then, is to act promptly when the first case occurs, and not on any account to allow the resulting 'crop' to develop in school.

When measles occurs in a house, the question may arise as to how far it is necessary to exclude the children from school. On this point admirable rules have been suggested by Thomas for the London County Council: (i) A child attending other than an infant school, who has already had measles, need not be excluded; (ii) a child attending other than an infant school, who has not had measles, must be excluded till the Monday following the expiration of fourteen days from the occurrence of the first case; (iii) a child attending an infant school, whether or not it has had measles, is excluded for the same period.

The control of measles in large boarding schools, such as the English Public Schools, has on several occasions been the subject of interesting discussion. Several school medical officers, notably Dr. Armstrong of Wellington College, have gone so far as to doubt the advisability of attempting to control the spread of measles even if it were possible. He holds that the larger the epidemic the more numerous the complications and the greater the case mortality. Success in stopping an outbreak only means that a greater number of susceptibles will be exposed to the next importation of infection. It has been found that, when a third of a school is susceptible, what may be termed an 'explosive mixture' results. In such a mass of unprotected material the infection spreads with great rapidity, and in consequence the patients are apt to be overcrowded unless very careful provision is made in advance. For instance, Dr. Lemprière reports that in one epidemic 112 out of 125 unprotected boys were attacked, and that the largest number of beds occupied was 109 on the 30th day. Under these conditions the available floor space was 80 square feet per head, or less, and few of us with hospital experience of measles would be surprised if results were occasionally unsatisfactory with such overcrowding.

It has been mentioned above that many good authorities doubt the necessity of *disinfection* either of the school or the home after measles. Domestic cleaning is held by Newsholme to be all that is necessary in the latter. We still disinfect the clothes of measles patients in Edinburgh, but there is, so far as I am aware, no reason to believe that the omission of this

precaution would be attended with bad results. As regards *isolation* in hospital it cannot be justified as a means of limiting infection, but it is of the greatest value in saving the lives of the children of the poor. The period of detention in hospital is determined more by the condition of the patient and the dread of complications than by the fear of infectivity. Return cases of measles are unknown. Our minimum detention of children is a fortnight, but adults, if apparently well, can be discharged with safety ten days from the appearance of the rash.

Although in the opinion of the medical officers of some of our great boarding schools it would be advantageous that boys should have passed through an attack of measles in their preparatory school stage, I think most will agree that measles should be postponed, broadly speaking, as long as possible, and that special efforts at least should be made to protect children below five years of age. No one should be wilfully exposed to the infection of measles to save trouble. The medical attendant must insist on taking precautions to prevent infection, even when he is morally certain that the mischief is already done.

Specific prophylaxis. Interesting experiments in immunization have been recently carried out in America by Richardson and Connor. The method is the intramuscular injection in doses of about 15 c.c. of an immune serum which is obtained from convalescents, the blood being taken some time between nine and twenty days after the eruption. Of four children exposed, three, who were protected in this manner, failed to take the infection, whereas the fourth, who was used as a control and left uninoculated, contracted the disease. In the case of three other susceptible and exposed children, nasal and throat swabbings from measles patients were rubbed in the nostrils and fauces, and a dose of 25 c.c. of immune serum was injected simultaneously with a view of securing an active immunity. None of these children developed measles. It is unfortunate that the inoculation of monkeys, which was undertaken by Sellards and Wentworth with a view to carrying out experiments in prophylaxis, failed to give satisfactory results. The susceptibility of these animals to the disease seems very variable; otherwise it might be possible to obtain an effective prophylactic serum from them.

CHAPTER III

RUBELLA

Etiology.	Desquamation and Convalescence: complications.
Dissemination and Infection.	
Predisposing Factors.	Mild and Severe Types.
Incubation Period.	Prognosis.
Invasion Period.	Diagnosis.
Period of Eruption: the rash, catarrhal symptoms, temperature, glands.	Treatment.
The Blood: the urine.	Prophylaxis.
	Note on Fourth Disease.

Synonyms—German Measles, Epidemic Roseola, Epidemic Rose Rash. *French*, Rubéole. *German*, Rötheln.

AETIOLOGY. There can be no doubt that rubella depends on a specific virus. The old theories that it was either measles or scarlatina in a modified form, or a hybrid between the two, can be no longer entertained. The disease breeds true. It causes neither measles nor scarlatina in those infected by it, nor does an attack of it protect against either of these fevers. On the other hand, one attack is sufficient to protect against a similar infection in future. Again, to have had either scarlatina or measles, or both, is no protection against rubella.

The disease occurs in epidemics, and the cases, while showing more variation in type and characteristics than is the case with the other exanthemata, have symptoms sufficiently uniform to leave no doubt about their specific character. Much confusion has arisen in the literature owing to all sorts of conditions having been from time to time described as rubella. Mild cases of scarlatina, and cases of scarlatina and measles coexistent in the same patient, have certainly been called German measles, and so probably have various forms of erythema. It is this confusion which is chiefly responsible for widely differing accounts of the disease, especially with reference to its mortality. Another source of difficulty is that it has not been by any means proved that two or perhaps more infective conditions of this nature do not exist. Dr. Clement Dukes has described a *Fourth Disease* in which the symptoms resemble mild scarlatina, but which, he holds, is a distinct entity. Personally, I cannot feel he has proved his case, but I am far from asserting

that we may not ultimately distinguish a fever the main characteristics of which more nearly resemble those of a trivial attack of measles. Rubella itself is probably the 'morbilli sine catarrho' of the old writers.

Rubella is not nearly as infectious as measles, but is, in my opinion, more infectious than scarlet fever. The *infection* is extremely short lived, and probably lies in the catarrhal discharges of the nose and throat. The short time that the catarrh lasts, in comparison with that of measles, no doubt does much to limit the amount of infection caused. It is extremely improbable that rubella can be conveyed by a third person, and it is doubtful if *fomites* play any part in the dissemination of the virus. The disease is common both in Europe and North America. The spring and early summer seem the most usual *season* for epidemic prevalence. In Edinburgh we see most of our cases in April and May. While a year seldom passes without a few cases being admitted to hospital, more extensive epidemic outbreaks occur every three or four years. As regards *age* it is impossible in a disease which is not notifiable to obtain satisfactory figures, and, as there is no mortality, no assistance can be obtained from death returns. Our hospital records are vitiated by the fact that children are often kept at home, whereas adult lodgers and servants are sent into hospital. I find that an analysis of 1,000 patients, who had rubella on admission to hospital and who did not contract the infection with us, shows that nearly a quarter were under five years of age and 551, or considerably more than half, were in the first ten years of life. The next two decennial periods furnished 202 and 197 respectively, and twenty-seven patients were between the ages of thirty and forty. Seven patients were over the age of forty years, three of them exceeding fifty, and in a more recent series of cases patients of over forty were not very uncommon, the oldest being fifty-nine years. Indeed rubella appears to attack adults much more commonly than is the case with the other exanthemata, always excepting small-pox. So far as my observations go, *sex* does not exert any influence.

INCUBATION PERIOD. This is distinctly longer than the corresponding periods in measles and scarlatina. I believe it in most cases to be eighteen days from the moment of exposure to the appearance of the eruption. As, however, a fairly well-marked prodromal period often exists, the incubation may be in reality considerably shorter than the above figure. In a recent group of cases I found the period up to the moment of the first symptom varied from fourteen to twenty days, in the majority of instances being nearer the lower than the higher number, fourteen, fifteen, and sixteen days being the most frequent figures. I have not personally met with a period of less than thirteen or more than twenty days. Instances, however,

of a twelve-day incubation have been reported by Clement Dukes and by Brownlee, both most careful observers. For practical purposes we may consider that rubella takes from twelve to twenty-one days to develop, and that probably at least two-thirds of the total cases have an incubation period of from fourteen to eighteen days. It will be necessary, then, to impose a quarantine period of three weeks at least upon susceptible contacts, should their isolation be insisted on.

INVASION PERIOD. The symptoms of this period are so extremely slight that it is not at all unusual for the rash itself to be the first obvious manifestation of the disease. It is, in fact, most unlikely that medical aid will be sought before the appearance of the exanthem. But it is beyond all question that a prodromal period does exist, and, as the patient is probably most infectious in this early stage, its recognition is of considerable importance in limiting the spread of infection by contacts. As the result of a careful inquiry into the history of the early symptoms of 153 consecutive cases of rubella, chiefly adults who were able to give an intelligent account of their illness, I found that no less than 101, or exactly two-thirds of the whole, had suffered from prodromal symptoms for a period varying from twelve hours to a week. It is true that in nearly half of these patients the symptoms were only present for twenty-four hours before the eruption was noticed, but the prodromal period lasted two days in eighteen cases, three days in twenty-one, four days in seven, and from five to seven days in the remaining eight patients.

The most frequent symptom noted in this period of invasion is unquestionably slight catarrh, which occurred in more than half of my cases. The patient suffers from a cough, which is rarely troublesome, and sneezes more or less frequently. On the other hand, there is seldom actual running of the eyes or nose, although the catarrh may in some instances be sufficiently well marked to cause such symptoms. About one-fourth of my patients complained of some slight degree of sore throat. This was occasionally the only symptom noted, though usually it was found in conjunction with the catarrhal symptoms. Headache was noted in one-third of the cases. It was seldom severe. A general feeling of malaise, with no definite complaint, was experienced by several, and a slight feeling of nausea is not an uncommon symptom. Vomiting, on the other hand, is not very common. In a recent series of 500 cases it was present in exactly ten per cent. and always as an immediate precursor of the rash. Shivering and feelings of chilliness occasionally occur. As, however, a considerable proportion of these patients were notified as scarlet fever, perhaps in consequence of these very symptoms, and would otherwise have been kept at home, it would be

unwise to assume that vomiting and shivering are to be regarded as comparatively common signs.

The most interesting feature, however, of this period is the glandular enlargement which is not infrequently noted even at this early stage. Several of my patients noticed that their cervical glands were markedly enlarged, sometimes a full week, but usually only two or three days, before the exanthem appeared. No less than one-fourth of the adults complained of *stiff-neck* from this cause, and there is no doubt that a systematic examination of the cervical, occipital, and axillary glands of contacts, in a school epidemic, for instance, would do much to secure early isolation, and, as a result, tend to limit the spread of infection. My friend, Dr. Hunter Paton, has had admirable results from this method in the large girls' school at St. Andrews.

PERIOD OF ERUPTION. As has been said above, it is not until the rash manifests itself that the average case is likely to come under the notice of a medical man. The face is usually affected first, spots appearing on the brow, about the roots of the hair, and behind the ears. The individual spots are considerably larger than the punctate spot of scarlatina and, even in the most profuse rashes, much less closely set together. On the other hand, they are more definitely circular and much less raised than the measles papule, and in most cases they are distinctly smaller. There is much less tendency than in measles for the spots to coalesce into irregularly shaped macules, although at times the rash may present quite a blotchy appearance on the face and forearms. Should this be the case the resulting macule is much less elevated than those caused by the coalescence of measles papules, and indeed is seldom appreciably raised above the level of the surrounding skin. The spots invariably invade the circumoral region, and may be numerous in that situation even when very discrete on the rest of the face. It must be noted, however, that the eruption on the face is often disappointing, and that in male adults especially it may scarcely be visible. I have been much struck by the apparent freedom of the face in soldiers and sailors with sunburnt and weather-beaten skin, the rash being perhaps too delicate in tone to make any show on such a background. From the face the exanthem spreads rapidly to the trunk and arms, the legs, as in the case of the other eruptive fevers, being last affected. In my experience, when the rash first invades the trunk it consists of very discretely scattered circular spots, but this appearance is soon lost when the spots become more numerous and the clear definition of the margins of the individual macules becomes less distinct. Very often, indeed, the effect becomes that of an almost uniform scarlatinal flush. As, by the time this occurs, the rash has often entirely





disappeared from the face, leaving absolutely no staining behind it, the general aspect of the patient may strongly suggest scarlatina, especially as the circumoral region often stands out clear and white against a somewhat flushed face. The upper and lower extremities may also present a scarlatiniform appearance, though it is more usual for the rash in these situations to suggest rather a morbilliform type. A patient with rubella seldom, in fact, shows an eruption which presents the same appearance all over the body at once. The rash, moreover, is apt to show different degrees of intensity in different parts of the body at the same moment. It is practically never equally bright in all situations. This multiform character is one of its most interesting and well-marked features. It may also be noted that in some patients even a well-developed eruption fails completely to invade the legs.

In some epidemics, it is said, all the cases may be of a scarlatinal type, whereas in others the spots remain quite discrete, and there is no resemblance to scarlatina. I have certainly seen many cases in which the rash never became scarlatiniform, but in most patients the eruption runs the course described above. Careful inquiry will nearly always elicit the fact that the rash commenced with a crop of discrete spots on the face. These, however, have often disappeared before the patient is examined by a medical man.

Stress is laid by many authorities on the *itching* which may accompany the eruption. It is probably a more frequent symptom than in either measles or scarlatina, but many patients do not complain of it, and I have not found it of any value in diagnosis. The question of *colour* is much more important. It is impossible to describe colour in words. That of rubella seems to lie somewhere between the bright red of scarlatina, and the decidedly bluish pink of measles. I should personally call it a somewhat 'faded' red. Those who have seen a sufficient number of cases of the three diseases will find it most useful in diagnosis.

As regards the *duration* of the rash there is much variation; an average period of eruption would be from twenty-four to thirty-six hours, but occasionally the rash only lasts about twelve hours, and I have seen it persist for as long as four and a half days. Should it last long, it varies very much in distinctness, having a great tendency to almost disappear and to return again, and being particularly bright and persistent on those parts of the body which are kept warm. I have often resuscitated an almost faded rash by packing the patient in blankets and hot bottles.

With the rash there is usually a certain amount of catarrh. More than two-thirds of the cases sneeze and cough occasionally, though as a rule these symptoms are so slight that they cause the patient little or no inconvenience.

Running at the nose is rare. The eyes are never badly affected. The 'bleary' appearance, so frequently noticed in measles, does not present itself in rubella, nor is there photophobia. On the other hand, the conjunctiva is frequently sufficiently injected to give a pink colour to the white of the eye, and not infrequently the patient will complain of some smarting of the eyes. Up to quite recently I never observed the laryngeal symptoms described by Cheadle, and I still believe that laryngitis must be regarded as very rare and only as a complication. But among the hundreds of soldiers and sailors who came under my observation during the war three suffered from persistent laryngitis which either appeared with the rash or very shortly after it. It is interesting that all these men were Australasians, and that the cases did not occur in one outbreak but in quite separate epidemics in different years. In no case was there any doubt about the diagnosis.

The fauces are usually more or less congested, and the majority of patients complain of slight *sore throat*. The soft palate may be slightly injected and occasionally shows some dusky spotting and even fine vesiculation. Very similar appearances, however, may be seen in measles, and small vesicles are not unknown on the palate of scarlet fever. The buccal mucous membrane in the vast majority of cases is entirely unaffected. In a few instances, however, I have found it slightly congested. The tongue presents no special features. It is usually clean or only slightly coated. The fur shows no particular tendency to desquamate, as in scarlatina, and the papillæ are not unduly prominent.

The **temperature** is usually moderately affected, although some patients, even with well-developed rashes, appear to suffer from no pyrexia at all. It is probable, however, that in the vast majority the temperature rises to 99° or 100° F. at the moment the rash appears. From this level it often regains the normal before the rash fades. In 500 consecutive patients the temperature exceeded 101° in twenty-six cases, in three reaching 103°, and in seven 102° or over. In the more severe cases, then, the temperature is sometimes well marked, but it may be said that as a rule the pyrexia is quite disproportionate to the amount and brilliance of the rash. The pulse and respiration may be accelerated in proportion to the rise of temperature. If fever is well marked, the patient suffers from some general discomfort and malaise, and may complain of pains in the back and limbs. But, as a rule, he feels practically well, and it is difficult to persuade him to remain in bed. In the case of children particularly, their brightness and good spirits, even when covered with a profuse eruption, is sufficient in many cases to distinguish the disease from the more severe exanthemata.

✓ The characteristic enlargement of the **glands** is present from the first

signs of the rash. As has been said above, it may even precede the rash by several days. The glands most constantly affected are those lying along the posterior border of the sterno-mastoid muscle, where they may not infrequently be seen and can nearly always be palpated without difficulty. They are felt as a chain of small bullet-like masses, rolling easily under the finger, and showing no tendency to become matted together or fixed. The glands at the angle of the jaw are also very often enlarged, and less frequently the glands in the lower part of the neck and above the clavicle are also affected. The suboccipital glands are usually involved, and occasionally the swelling in this situation is very appreciable. I have seen glands in this situation each the size of half a walnut, and causing considerable discomfort to the patient. The mastoid glands often become readily palpable, but in my experience their enlargement is not so invariable as some authors have asserted. The axillary groups, on the other hand, are involved in the great majority of patients, the inguinal also frequently suffer, and enlargement of the epitrochlears may be sometimes appreciated. Some writers lay considerable stress on the tenderness of the affected glands. While it is undoubted that, when the enlargement is very marked, considerable tenderness may exist, my experience is that in the average case gentle palpation does not cause the slightest discomfort. The patient is not, as a rule, conscious of the adenitis, and it is only in about a fourth of the cases that there is any sensation of stiffness of the neck. This symptom, moreover, seems to be much more frequent in adults than in children. The glands never suppurate, and they usually subside with the same extraordinary rapidity with which they appear, seldom being appreciable after the rash has faded and often disappearing even earlier. I have, however, recently seen two medical men whom I had previously treated three years before for rubella and who assured me that in their case the occipital glands had remained permanently hard and enlarged, although previous to the illness neither had ever suffered from glandular enlargement.

The Blood. It is stated that in the majority of cases leucopenia is

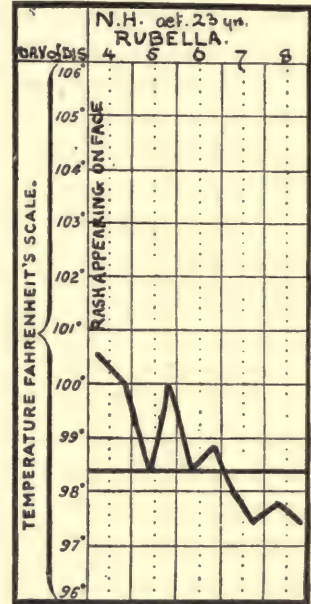


FIG. 8. Showing the trivial temperature of rubella in the eruptive stage. The patient had a history of stiff-neck for three days previously.

present, and that the minimum count is obtained on the third day after the appearance of the eruption. The neutrophile cells are very markedly reduced, absolutely and relatively, and there is a relative increase of mononuclears. One of my assistants, Lyon, in an unpublished thesis, made a study of the blood, and his results tend to show that, while leucopenia was present in about half the cases, in the remaining half there was a moderate leucocytosis. The most constant feature was a relative increase in lymphocytes, which, though occasionally below 40 per cent. on the first day of the rash, were invariably above 50 per cent. by the third day and averaged 55 per cent., the large mononuclears being much increased in numbers. In control counts of measles blood the polymorphs formed 57 per cent. of the cells.

The Urine. It is very unusual in my experience to find albumin in the urine, although outbreaks have been reported in which slight albuminuria is a common feature. It is most exceptional to find the diazo reaction present, and this may be a point of some diagnostic importance if we have to distinguish between rubella and measles, as in the latter disease the test is almost invariably positive towards the end of the eruptive period. In a recent series of 500 cases of rubella only two showed the reaction, and it is interesting that one of them, although I decided after some hesitation to diagnose it as rubella on its general clinical features, had been demonstrated to students on admission as a doubtful case. The other, though diagnosed as rubella by a most competent practitioner, only presented a faded eruption on the lower extremities on admission, and could hardly be regarded as a certain case. I am inclined, therefore, to employ this test in the future as a means of diagnosis. Hitherto I have been endeavouring to estimate its usefulness by observing it in already diagnosed cases.

PERIOD OF DESQUAMATION AND CONVALESCENCE. After the disappearance of the rash there is usually a slight desquamation. There is seldom more than a slight furfuraceous powdering which is often well seen on the face. There is nothing of the nature of real peeling, and the palms of the hands are quite unaffected. The process lasts only a few days, and should in all cases be complete within ten days of the fading of the rash. Some authors describe a faint staining of a yellowish tint as persisting after the rash. This is, I think, rare, and in any case of no use in diagnosis. **Complications** either in the period of eruption or in that of convalescence are almost unknown. Cases of broncho-pneumonia, tracheitis, and bronchitis have been reported in various epidemics, but it is probable that they were merely accidental and in no way depended upon the virus of the disease itself. The same might possibly be said of the rare cases of laryngitis

noted in a preceding paragraph. Otherwise I have never seen complications occur either in the course or convalescence of rubella, with the exception of neuralgia and toothache, always in adults, which I have noticed sufficiently frequently to incline me to the belief that enlarged glands may in some way have pressed upon the affected nerves, and of one case of double otitis which may well have been due to some other cause. *Relapses* undoubtedly occur occasionally. I have, however, never seen a second attack, though in this respect there is no reason to believe that rubella differs from the other exanthemata.

MILD AND SEVERE TYPES. Clement Dukes maintains that in some cases the rash does not appear and that the manifestations of the illness are limited to very slight catarrhal symptoms or to pinkness of the eyes alone, and Hamburger mentions cases in which glandular swelling was the only symptom. The rash is so very evanescent in many instances that it might well run its whole course in the night and escape observation altogether. I have never seen rubella of a severe type. It may, of course, be relatively severe with considerable pyrexia, but the patient never seems seriously ill. Most of the dangerous cases reported by the earlier writers on the subject would appear to have been in reality measles, scarlatina, or both these diseases co-existent in the same patient at the same time. On the other hand, Cheadle has given an account of a series of cases in which the rash was dark purple, and almost hæmorrhagic in character, and in which laryngitis and bronchitic conditions frequently occurred as complications. His patients had all suffered from measles previously; otherwise the description tallies more with an epidemic of the latter disease. I cannot, however, reconcile these cases with my own experience of rubella, and I think it probable that another infection, distinct from scarlatina, measles, and rubella, may have been responsible for this particular outbreak. Should that be so we should have to entitle it the Fifth Disease, as it does not in the least resemble the condition described by Dukes as the Fourth.

PROGNOSIS. If we may assume that Cheadle's cases were not instances of rubella, it may be said with confidence that the prognosis is uniformly favourable. Occasionally, however, an attack of rubella may precipitate the fatal termination in various wasting and prolonged diseases in children. I recollect a case of tubercular disease, for instance, in which we could only attribute the rapid change for the worse to an attack of rubella. There is no mortality, however, from the disease itself.

DIAGNOSIS. In times of epidemic the only difficulty will be with the diagnosis of the first two or three cases observed. The subsequent cases should be readily recognized. The history of exposure, the comparatively

long period of incubation, the slightness of the symptoms, and the polymorphous character of the eruption should make the diagnosis simple enough. But the recognition of a first case, especially if scarlatina, measles, or both should be epidemic at the time, may be a matter of considerable difficulty. If we can eliminate these two exanthemata, and at the same time satisfy ourselves that we are dealing with one of the infectious diseases, the diagnosis is made. Occasionally, however, we may have to distinguish the eruption from various adventitious and drug rashes.

i. The differential diagnosis from scarlatina is often extremely difficult. A patient with rubella is usually mistaken for scarlatina when he is seen on the second day of his rash, or, at any rate, after the spots have entirely disappeared from his face. By that time the circumoral ring is often perfectly clear and absolutely free from any trace of staining. The face may be flushed and the whole appearance of the patient may strongly suggest scarlatina. Usually, however, the eyes are slightly pink. It is true that the conjunctiva may be occasionally suffused in scarlatina, but this is only the case in patients who are suffering from a very severe form of infection, and who are not in the least likely to be confused with rubella. The eye in scarlatina is, as a rule, remarkably bright, and the conjunctiva quite clear. On examining the rash, which is often very scarlatiniform on the body, it will be found that it never presents the fine punctate spotting of true scarlatina. It is altogether more diffuse, and is more likely to present different appearances in different situations. On the arms, or on the inside of the thighs, for instance, it may be frankly morbilliform, or at least discretely spotted. Remembering that in all the exanthemata the rash on the legs is usually later in appearing than that on the body, a careful examination of the *dorsum of the foot* will often clear up any difficulty. The rash in this situation may be caught when it is comparatively fresh, and in many doubtful cases the characteristic discrete circular spots recognized on the foot and lower part of the leg, when the rest of the eruption had run together into a diffuse blush, have enabled me to make a definite diagnosis of rubella. There is, I think, no exanthem which it is more necessary to examine on every part of the body.

It is, of course, only the milder cases of scarlatina that are likely to be mistaken for rubella. The throat, then, seldom affords us much assistance. It is nearly always slightly congested in rubella. It is often no better marked in mild scarlatina. The dark spots on the palate, on which Förschheimer lays stress, are not by any means always present, and though I have seen often enough very minute vesicles in the same situation I am convinced they are not peculiar to rubella. The tongue is perhaps a better guide, as



RUBELLA.

The legs of the patient whose back is shown in Plate IV. Note the comparatively fine spotting on the dorsum of the foot.

the papillæ are often very prominent even in slight cases of scarlatina, and they are normal in the other condition. The presence or absence of albuminuria is of little or no value. Cases of scarlatina, liable to be mistaken for rubella, practically never have albumin in the urine. Should albumin be detected, one would be justified in assuming that in patients so slightly ill its presence is due to some cause totally unconnected with the condition under diagnosis. As regards the invasion symptoms of either disease, vomiting and shivering would certainly suggest scarlatina. But it must be remembered that both occur in a small proportion of cases of the less severe disease. On the other hand, catarrh, however insignificant, points strongly to rubella, and the history of even a single sneeze should not be lightly put aside. Scarlatina patients very rarely sneeze unless they have a nasal discharge, and the septic cases, in which that occurs, are too well marked and too severe to be confused with rubella. A history, which may often be obtained, of distinct spots having been noticed previously on the brow or round the mouth would entirely eliminate scarlatina. Marked glandular enlargement and, above all, complaint of stiffness of the neck are also points in favour of a diagnosis of rubella, but, as will be seen below, the value of glands as an aid in coming to a definite decision has its limitations. If a definite diagnosis cannot be arrived at, the case always should be regarded as one of scarlatina until it is found that the characteristic desquamation of that fever, so unlike the mealy powdering of rubella, does not occur.

ii. To distinguish the disease from a mild attack of true *measles* may be also a matter of extreme difficulty. In making this differentiation the history of a well-marked catarrhal period lasting several days is of course in favour of measles, as, although such a period frequently exists in rubella, its symptoms are so trivial that they are hardly noticed by the patient or his friends. In measles, on the other hand, it is extremely rare not to find that very definite catarrhal symptoms have existed for at least two days before the appearance of the rash. A history of stiff neck is in my experience unknown in measles. We have seen that it may be complained of with comparative frequency in rubella. This is also the case with sore throat, a complaint very rarely made by measles patients. As regards the actual appearance of the patient, even the mildest cases of measles present more marked conjunctival symptoms than are to be found in rubella, in which latter disease, it may be said, lachrymation practically never occurs. Troublesome and frequent coughing and sneezing, laryngeal symptoms, and running at the nose would all point to true measles, even if the temperature is trivial and the constitutional disturbance not great. The cases of rubella

liable to be confused with measles are, of course, those in which, at the moment of examination, the rash has not disappeared from the face. While as a rule the very discrete circular spots of rubella show much less tendency than the measles papules to run together into irregularly shaped blotches, on the face and arms there is occasionally a sufficiently blotchy appearance to render the diagnosis very difficult. There is, however, much less elevation of the macules than in measles, and, by those who have had experience of the two diseases, a difference in colour will be appreciated. When the rash has faded from the face the differential diagnosis becomes much easier, for measles always leaves more or less staining on the face and round the mouth, whereas it is just at this period in rubella when the clear circumoral ring suggests scarlatina. The rash on the trunk also by this time should be becoming more diffuse, and one never sees the comparatively large areas of staring white skin which are nearly always to be found here and there even in the most run together and brilliant measles rashes. The underlying skin is in fact more generally pink, and the edges of the spots much less well defined, the patient presenting an irregular flush of varying intensity. Even if the rubella rash does not invariably become diffuse, I have never seen much tendency for the discrete spots on the trunk to coalesce in groups, and well-marked macules in this situation, whether crescentic or otherwise, would certainly, other things being equal, suggest measles. As in scarlatina, the examination of the parts where the rash is likely to be most recent will often settle the question, and it must be remembered that the measles rash is as a rule extremely uniform, while that of the less severe disease varies much in different situations at the same time. Certain cases of measles may, it is true, show large areas of confluence on the back which may give a sort of polymorphous character to the rash, but in my experience these cases are usually too well marked to be mistaken for rubella.

Perhaps, after all, the most reliable assistance is to be obtained by a careful examination of the mucous membranes of the mouth. Should definite Koplik's spots be recognized the diagnosis is made. These spots do not occur in rubella. But apart from the presence of actual spots it may be broadly stated that, whereas the buccal mucous membranes in measles are always dirty looking and inflamed, in rubella they are practically normal. The palate, however, may show some spotting in both diseases. As indicated above, a positive diazo reaction is a strong point in favour of measles. A negative reaction, if the examination is made when the rash is beginning to fade, is an even stronger argument in favour of rubella.

iii. *Various adventitious rashes* due to drugs, to articles of diet, to

enemata and to similar causes, may also occasionally give trouble in diagnosis. The two main characteristics of such eruptions, firstly their polymorphous appearance and secondly the fact that they cause little or no constitutional disturbance, while of value in distinguishing them from the more severe exanthemata, only make their distinction from rubella more difficult. Many of these rashes, however, show patches of urticaria, others may present a circinate arrangement, and such appearances are never met with in rubella. In a doubtful case the history of catarrh, however slight, or the presence of characteristic glands should turn the scale in favour of the infectious disease. On the other hand, a careful inquiry into the possible causes of a doubtful rash may often clear up a difficult case. Antitoxin rashes seldom resemble rubella, and, except in the case of a patient who is known to have been exposed to infection, it is unlikely that any confusion could arise. I have had most trouble with rashes in young children at the period of dentition, who occasionally present on the trunk a diffuse spotting of a colour not unlike that of rubella. Here again, unless there is a special reason to suspect infection, the age of the patient and the probability of gastric disturbance is usually sufficient to explain the rash. It may also be mentioned here that, with the influx of naval and military patients during the war a fair number were found to be suffering from syphilitic roseola.

It has been hinted above that in differential diagnosis it may be unwise to lay much stress on the condition of the glands. The occipital, mastoid, and cervical glands are all liable to be enlarged in irritative conditions of the scalp. To trust, then, to glands in these situations we must be certain the patient has a clean head, free from eczema, sores, or pediculi. The inguinal glands in children may also be enlarged owing to want of cleanliness. The result is that in hospital patients it is wiser to pay most attention to the glands in the axilla. In good-class practice this fallacy should be reduced to a minimum, but I must confess to having discovered pediculi in the most unlikely children. Again, the glands are often well marked in scarlatina and in measles. An absolute absence of palpable glands, on the other hand, is a strong presumption against a doubtful case being one of rubella.

It may not be out of place here to emphasize the nature of the *stiff-neck* so often complained of by adults. Owing to the sudden great increase in the size of the cervical glands there is a certain discomfort in moving the head. In one week two naval patients were sent into hospital, one notified 'cerebro-spinal meningitis' and the other 'rubella'. Both had complained of stiffness of the neck, but it was the former case which proved to be

rubella and the latter meningitis. It is perhaps hardly necessary to say that nothing resembling the spasmodic rigidity of meningitis occurs in the milder infection, but this curious experience has led me to believe that it may be useful to mention the point.

TREATMENT. In an illness which is invariably benign, and in which it is difficult to persuade the patients that there is anything wrong with them, it is obvious that there is not much scope for therapeutics. It is advisable to keep the patient in bed during the period of eruption and for two or three days thereafter. Should there be pyrexia, a light diet is requisite. If, on the other hand, there is no fever, there is no reason why an ordinary diet should be withheld. It is seldom that the cough is sufficiently marked to require treatment. While, as a general rule, I have been in the habit of employing an **isolation** of ten days, I have no reason to believe that the infection lasts so long, and on occasion I have allowed patients to leave the hospital five or seven days after the appearance of the rash with no bad results. If the weather is good hospital patients can be safely allowed out in the grounds two days after they have been permitted to get up.

PROPHYLAXIS. The infection is very short-lived and it is doubtful if energetic measures to destroy it are necessary. The thorough airing of the rooms occupied by the patient and a good cleaning are probably sufficient. In school outbreaks I should be content with keeping susceptible contacts away from school from the tenth to the twenty-first day after the date of their exposure. Should this not be deemed desirable, a very careful attention to the state of the glands of contacts, and the prompt isolation of any children showing even the slightest catarrh, will probably do much to limit the chance of a 'second crop'. Quarantine for the full period of three weeks seems far too drastic a method of dealing with so mild an infection, but, should it be insisted upon, it should be limited to persons who have not had the disease before. The chance of second attacks is too insignificant to be considered.

NOTE ON THE FOURTH DISEASE. At the time Dr. Dukes first published his account of this condition, not a few practitioners were inclined to agree with him, and to hold that a condition closely resembling mild scarlatina, and yet distinct from that fever, from rubella, and from measles, did in reality exist. In many instances, however, the evidence brought forward was obviously insufficient, and cases of rubella with scarlatiniform rashes, instances of relapse after scarlatina, and very mild outbreaks of scarlatina itself, were alleged to be 'Fourth Disease'. The symptoms ascribed to the illness by Dukes himself were a bright scarlatinal rash, not

apparently invading the face; a swollen throat; some enlargement of glands, moderate pyrexia, and pink eyes. The incubation period appeared to be from nine to twenty-one days. Desquamation was sometimes very slight; sometimes as profuse as in scarlatina.

With all the large amount of material at my disposal I have never satisfied myself that, if a fourth disease exists, it is of the type described by Dukes. The view expressed at the time by Washbourn and others was that some of the cases were rubella, and others mild scarlatina. In any case no definite outstanding features distinguished the patients described from persons suffering from one or other of these conditions. The difficulty of diagnosing rubella is often great, and, on the other hand, we shall see that scarlatina often presents extremely trivial symptoms. We may conclude with the remark that the so-called Fourth Disease is not accepted as a definite entity by the most competent judges.

CHAPTER IV

SCARLET FEVER

Etiology : predisposing factors, susceptibility, dissemination, infectivity.

Bacteriology.

Morbid Anatomy.

Period of Incubation.

Period of Invasion.

Period of Advance and Eruption : temperature, facies, rash, throat, tongue, glands, urine, blood.

Period of Defervescence and Desquamation.

Types of Scarlatina : mild forms, severe forms, toxic, septic, typhoid, surgical, puerperal.

Relapses and Second Attacks.

Complications : nephritis, arthritis, adenitis, otitis, rhinitis, vaginitis, &c., &c.

Post-scarlatinal Diphtheria.

Diagnosis : differential diagnosis from tonsillitis, diphtheria, influenza, measles, rubella, small-pox, drug rashes, serum rashes, enema rashes, food rashes, &c., &c.

Prognosis.

Treatment : management and general treatment, diet, local treatment, treatment of septic cases, toxic cases, serum treatment, vaccine treatment, and treatment of complications.

Prophylaxis.

Synonym—Scarlatina. *French*, Scarlatine. *German*, Scharlach.

ETIOLOGY. Scarlatina is no doubt due to infection by a micro-organism. It occurs in epidemic waves, and is also endemic in most of our large cities. It has been known to occur in all latitudes, and *climate* does not apparently exercise much influence, but the disease is, nevertheless, rare in Asia and Africa. It has been said that Anglo-Saxons are particularly susceptible to it, and it is extremely common all over northern Europe. Epidemic prevalence is undoubtedly influenced by *season*. In Great Britain the largest number of cases are notified, and the most deaths occur, in the autumn months, the crest of the wave being reached in October, while the months of February, March, and April usually furnish the fewest cases. Up to the present time, however, we know very little about the effect of weather and temperature conditions upon the prevalence of the disease. An epidemic suddenly abates, often quite unexpectedly and with no apparent relation to meteorological observations. In cities, where the disease is endemic, it often assumes epidemic prevalence at intervals of about five years, and it is said to present an even better marked epidemic wave every thirty years. As regards *age*, scarlatina chiefly attacks the young, but at a slightly later period of life than is the case with whooping-

cough or measles. The greatest number of patients are in the second five years of life, and if each year is considered separately, Brownlee shows that the sixth year provides the largest number of cases. The number of infants of under one year who contract the illness is relatively small. The fever is common enough in the second year, and the numbers affected are much increased in the third, after which time there is a moderate but steady increase to the sixth. Thereafter there is a decrease with each succeeding year, and after the age of fifteen the cases commence to be relatively few in number. The infection, however, can be contracted at any time of life, although out of no less than 167,840 cases tabulated by Foord Caiger, only eleven occurred in persons of over sixty, and only seventy-seven over fifty years of age. Some years ago I had under my care a man of 74, the only septuagenarian in a series of over 20,000 cases. *Sex* does not seem to have much influence, but females appear to be attacked slightly more frequently than males, particularly after the age of ten years.

Susceptibility to scarlatinal infection varies very greatly. Some persons, indeed some families, seem to be absolutely immune, although perhaps frequently exposed. On the other hand, members of one family may show a special predisposition to take the disease badly. Any lowering illness is liable to increase the chances of infection, and inflammatory conditions of the throat, particularly diphtheria, make the contraction of scarlatina more probable. It has been stated that puerperal women are peculiarly predisposed to the infection, but there can be little doubt that septicæmia accompanied by an erythematous rash is not infrequently mistaken for the fever, and I have seen so few instances of scarlatina in women recently confined that it seems unlikely that their susceptibility to the disease is increased.

Dissemination. As a rule the infection is spread by *direct contact* from person to person. The virus is no doubt contained in the nasal and faucial secretions of infected individuals, and may be doubtless scattered on surrounding persons and objects in the act of talking. It is easy to understand that it may be readily spread among children by the common use of towels, handkerchiefs, and the like. Cases are not infrequently met with in which the infection has been conveyed through the medium of a third person, who has carried it on his clothes, or perhaps, as is the case in diphtheria, even in his throat. That such a carrier should be able to communicate the infection by means of a second healthy intermediary is conceivable, indeed instances of it have been described; but it is most unlikely and can for practical purposes be disregarded. Outbreaks of the disease are frequently the result of *milk infection*. A sudden rise in the number

of notifications, especially at a time of year when scarlatina is not usually epidemic, should cause the milk supply to be suspected, and suspicions will be strengthened if a large proportion of the patients consist of adults. I have noticed this peculiarity in several milk outbreaks both of diphtheria and scarlatina, and attribute it to the fact that adults, though they usually drink less milk than children, are, as a general rule, much less likely to be brought into close personal contact with individuals suffering from the fever, the great majority of whom are in ordinary circumstances young children. I am aware that the exact contrary is often stated in connexion with milk epidemics, and that an excess of juvenile patients is regarded as pointing to the cause being milk. It is quite possible that the fact that in Scotland raw milk is taken largely by adults with their porridge may explain my experience. The milk may be, and probably usually is, contaminated by some infected person engaged in its distribution or working at the dairy. A considerable number of outbreaks, including the one at Hendon to be alluded to later, have suggested the possibility of the infection being in some instances derived directly from the cow itself. Expert veterinary opinion, however, is unanimous against the view that cows are subject to scarlet fever, and it seems safer in the meantime to accept the theory of Savage that they merely play the part of 'carriers' of a human infection. It is easy to understand how cows with sores on the udders may be infected from a human source, and those of us who believe in the probability of healthy human carriers of scarlet fever are not much impressed by the argument that cows have been proved responsible for outbreaks, because no human source of infection could be detected at the incriminated dairies. There is no reason to believe that the disease is ever spread by water. As to the possibility of aerial convection our experience at the old City Hospital in Edinburgh was that, though our buildings were surrounded by lofty tenements literally packed with children, the fever was no more common in this population, living so close to scarlet fever wards which often contained over 300 patients, than it was in other districts of the same class in the city.

Fomites may play some part in the dissemination of infection. The clothes of a patient are certainly infectious, and may remain so for some time. It is unwise, however, to accept unreservedly the tragic stories, so frequently related, of infection clinging to clothes and toys for over 20 years and then breaking out when the articles are for the first time disturbed. There can be, doubtless, a possibility of clothes, bedding, toys, letters, and books retaining infection for some time, especially if they are excluded from light and air. But Nesbit has demonstrated recently by carefully tracing the books in a public library during a scarlet fever epidemic that in no case

could infection be brought home to this source although opportunities for it were numerous, and negative observations of this kind, when carried out as they were over an extended period, are more impressive than single positive instances, which may well be due to coincidence. Many of the stories of persistence of infection in houses, moreover, are discredited by the fact that the possibility of living carriers was not considered, and it is probable that the importance of fomites infection has been much over-rated. Chapin states that of 13,970 cases reported in Michigan only 335 were even attributed to fomites infection, and we have seen (p. 29) that his own experiment of dispensing with disinfection was not attended by any bad results. Infection, on the other hand, is very readily communicated by instruments used for the examination or treatment of the throat, and also by cups, spoons, and other utensils used by a patient.

Carriers of scarlatinal infection undoubtedly exist. Apparently healthy convalescents retain the power of communicating the disease to others for comparatively long periods, and Butler has shown that the infectivity of such individuals is intermittent and liable to be excited by such trivial causes as a cold in the head. On the analogy of diphtheria it is not too much to assume that the virus may be also carried by persons who have not suffered from the disease. While this cannot be proved until the germ of scarlet fever has been discovered, it would explain many instances of infection which in the meantime are attributed to cows, fomites, and so forth.

School infection does not appear to play as important a part in the spread of scarlet fever as in the case of diphtheria or measles. In Edinburgh the commencement of the terms of the day-schools does not as a rule markedly affect the number of hospital admissions, except perhaps in the autumn, at which time the disease is in any case on the increase. The medical officer of our school board does not consider that there is evidence that the schools spread the infection, and Brownlee, after a careful examination of the records of the Belvedere Hospital for seventeen years, concludes that they give no support to the view that scarlatina is largely disseminated through the influence of the schools in Glasgow.

It has been suggested that *domestic animals* may assist in disseminating scarlatina, either as 'carriers' or by actually suffering from the disease. The evidence in favour of this, however, is by no means convincing. Recently attention has been drawn to the fact that prevalence of scarlet fever synchronizes to some extent with prevalence of *fleas*. But, in spite of the interesting suggestion of the autumnal 'flea-curve', transference of the disease in this manner appears highly improbable.

Infectivity. The patient is unquestionably infectious from the moment of his first symptom, but the infectivity is greatest at the height of his fever. A case is, generally speaking, dangerous to others, in proportion to its severity, but very mild cases undoubtedly will cause infection. Infectivity lasts for a long period, and it is impossible to say with certainty when it ceases. The infective material is contained in the secretions of the fauces, and in purulent discharges, particularly from the nose and ears, but also, in all probability, from the vulva or from suppurating glands or wounds. The infectivity of the desquamated cuticle has been much discussed. It seems reasonable to assume that, so long as the patient himself is otherwise infectious, his skin is likely to remain so, or, at least, is very readily contaminated. On the other hand, there is no reason to believe that late desquamation, in the fifth and sixth weeks of the illness, is of itself infectious, if the patient is free from all catarrh and discharges, and if the whole surface of the body has been adequately disinfected. As long, however, as any inflammatory conditions persist, the patient is dangerous to others for many weeks, certainly twenty or more. Six weeks was for long considered to be the minimum period of detention in hospital, but many institutions have reduced it to four with no worse results. By the end of five weeks the cuticle has usually separated from all parts of the body except the feet, and desquamation in this situation may usually be disregarded. The whole question will be found discussed in another chapter in connexion with the so-called 'return cases' of scarlatina, those cases in which a person has been infected by a patient recently discharged from hospital.

BACTERIOLOGY. In the meantime, we have no certain knowledge regarding the exciting cause of scarlet fever. There is a considerable amount of evidence in favour of a streptococcus. In 1885 an outbreak of the disease was traced to the milk from a farm at Hendon, and it was discovered that the cows were suffering from an eruptive disease of the udder. Klein, who made the bacteriological investigations, succeeded in isolating a streptococcus both from the patients and the cows. This micro-organism differed in certain particulars from the streptococcus pyogenes. In 1891 Kurth described a streptococcus the main peculiarity of which was that it tended to conglomerate in broth cultures. Since that time Baginsky and others have attributed scarlatina to streptococcal infection, and more recently Mervyn Gordon has made an elaborate and masterly investigation of the whole subject. He found that in the faucial secretions of scarlatinal patients two forms of streptococcus could be usually identified. One of these was identical, both morphologically and culturally, with the streptococcus pyogenes. The other, which was only found in scarlatinal cases and not in normal

controls, had certain cultural distinctions, prominent among which were its capacity of clotting milk and its conglomeration in broth cultures. In these respects it resembled the organisms described by Klein and Kurth. It also tended to form bacillary elements and spindle shapes when cultivated in solid media. For the further identification of the germ, its action on saccharose and different sugars has also been observed, and Gordon seems to find little difficulty in accepting it as the causal micro-organism, under the name of *streptococcus scarlatinæ* or *conglomeratus*.

The whole subject is beset with special difficulty on account of the fact that everybody recognizes that many of the worst symptoms of scarlatina are due to streptococcal infection, and that most of the deaths from the disease are due to that cause. And in these fatal cases there are no lesions which might not be readily expected to follow infection with the streptococcus pyogenes. On the other hand, it is at least a suggestive fact that a distinct variety of streptococcus should be found to occur in a very high percentage of even mild cases of scarlatina, and that it should have been successfully recovered from patients dying as early as the second day of illness. It is from these cases that we would expect to obtain the real cause of the infection, as secondary septic conditions do not develop, as a rule, in such toxic cases. On the other hand, the streptococcus which Baginsky cultivated from these rapidly fatal cases was not, in his opinion, distinguishable from other streptococci, although, as Gordon notes, it resembled that of Klein in its capacity to coagulate milk. Gordon does not state how long the ten fatal cases examined by himself survived. If they were of the 'toxic' type, it would, I think, enormously strengthen his case. It is hard to resist the conclusion that 'septic' scarlatina is due to a secondary infection, and that, quite probably, with the streptococcus pyogenes. But that in no way precludes a different variety of streptococcus causing the original infection. The intimate relations of the streptococcus to scarlet fever have been further demonstrated in recent years by the discovery in the blood of opsonins and complement-deviating bodies for streptococci. Streptococcal vaccines, moreover, have been said by certain Russian observers to confer an undoubted, if not absolute, protection against the fever, and it is asserted that in 10 per cent. of the cases they cause a general scarlatinal eruption with angina and strawberry tongue. American workers have, however, failed to observe such a phenomenon, which, if uncontradicted, would certainly have suggested the etiological importance of the streptococcus. While treatment by means of anti-streptococcal serums has been extensively employed, its success has hardly been sufficiently striking to justify it being adduced as an argument in favour of a streptococcal etiology, and such as it is may be readily explained

by the admitted frequent presence of the streptococcus as a complicating agent.

Other micro-organisms have been described as the cause of scarlet fever, but none of them have found much general support. I can find no recent work in confirmation of the claim of Class that the fever is due to a diplococcus, except that of Mair, who claims that such a micro-organism can be recovered from the throat of scarlet fever patients in the first week of the illness in 87 per cent. of cases. Mair also found that monkeys inoculated with this diplococcus developed symptoms resembling scarlet fever, including arthritis. Mallory and Medlar attribute the infection to a Gram positive bacillus. We may presume that the protozoon, the so-called 'cyclaster scarlatinalis', originally described by Mallory, has no further evidence in its favour. Döhle has claimed specificity for the inclusion bodies found in the polymorph cells and has reported the presence of a spirillum in the blood, but other observers have not supported him. Other intracellular bodies, also seen in the protoplasm of the neutrophil polymorphs, but differing from those of Döhle, have more recently been described by Amato, who considers they are parasites. Interesting inoculation experiments on anthropoid apes carried out by Levaditi tend to show that a modified form of scarlet fever may be given to these animals, but no causative organism seems to have been identified in his researches. The virus used for the inoculations was derived from the tonsillar exudation, blood, and glands of patients. Quite recently it has been suggested that the real cause of the disease will prove to be a filter-passer and possibly ultra-microscopic.

MORBID ANATOMY. In those very fatal cases of scarlatina of the toxic type which arrive early at a fatal termination, there is but little to be seen at a post-mortem examination. There is well-marked cadaveric lividity particularly in the dependent parts. The blood is dark and fluid. The viscera present the ordinary changes which are common to all acute fevers. In more prolonged cases the evidence of septic infection may be marked by the condition of the throat, the swollen or suppurating glands, and inflammatory conditions of the joints. In septic cases more or less bronchopneumonia is usually present, and pus can be squeezed from the small tubes. Endocarditis and pericarditis may occasionally be observed. The most characteristic scarlatinal lesion is the inflammatory change in the kidney, but this is often wanting. My experience, indeed, has been that septic cases running to a fatal termination seem seldom to develop nephritis. On the other hand, nephritis occurring in an ordinary case usually tends to recovery, and therefore it is not so common to see this condition upon the post-mortem table as might be expected. The kidney is usually slightly increased in

size, and the capsule strips readily. The cortex is pale, somewhat enlarged, and often fatty. The malpighian bodies appear as yellowish dots. On microscopic examination the principal changes are seen in the glomeruli, but occasionally the interstitial tissues seem to suffer most, and they are always to some extent affected. The tufts are congested, and there is proliferation of the cells lining the capsules and the tubules. The tubules themselves are filled with cells. The general infiltration of the tissues with leucocytes also helps to obstruct them.

PERIOD OF INCUBATION. It may be asserted with some confidence that the latent stage of scarlatina is invariably a short one. It is true that we read not infrequently of cases in which the disease is supposed to have taken from two to four weeks to develop, but these can be safely dismissed. The fact is that the estimation of an incubation period is beset with fallacies. When scarlet fever breaks out in a house three weeks after the removal of the supposed infecting case, it is much more probable that it is the result of some human carrier or a 'missed' mild case of the fever. Infection often clings to a family for long periods. Again, the difficulty of proving that the secondary case has not been exposed elsewhere to infection is usually very great. We may take it that the incubation period never exceeds seven days, and that it is very seldom

longer than four. The vast majority of patients take from two to three days to develop their first symptoms. It has been stated that an incubation of only a few hours is possible. In some cases I believe that the stage is certainly less than forty-eight hours, but anything under twenty-four must be extremely rare. Foord Caiger points out that the rash is delayed in some cases in which the incubation is said to have been specially short, and explains this by the possibility that the early throat symptoms might not depend upon scarlatina at all, but on some variety of tonsillitis, which would favour the subsequent development of the scarlatinal infection.

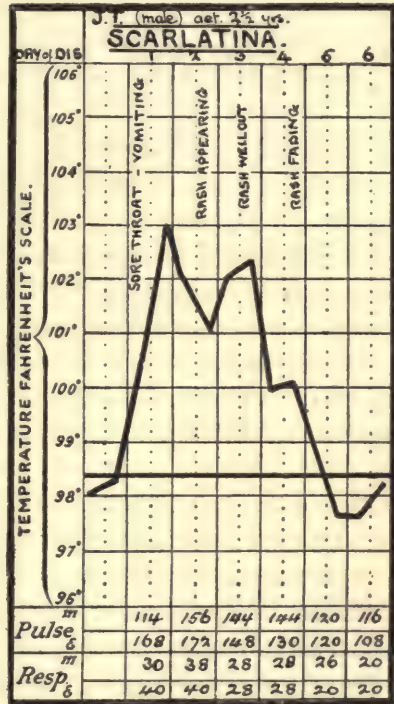


FIG. 9. Scarlatina simplex in a young child. Note rapid pulse at onset. First appearance of rash in thirty-six hours.

For twelve years, acting on the assumption that the period never exceeds seven days, I quarantined any ward, in which the disease had appeared, for that length of time from the removal of the last case. Although on one occasion the incubation stage was, so far as could be judged, as long as six days, in no instance was there any subsequent outbreak after the week had elapsed. More recently I have reduced the quarantine to five days with quite satisfactory results. Not only does this tell strongly in favour of a short incubation being the rule, but it enables us to feel confident that a seven days' quarantine period will be found amply sufficient for exposed children before they are allowed to return to school.

PERIOD OF INVASION. This may be said to last from the moment of the first symptom till the temperature reaches its height and the rash appears. The stage is usually a short one, seldom exceeding twenty-four hours, and often lasting less than six. In rarer instances the appearance of the rash may be delayed until thirty-six, or even forty-eight hours, have elapsed. The *temperature* rises, often with great rapidity, reaching a high level from the first in the majority of cases, though occasionally it may require two or three days to reach the acme. The *pulse* at this early stage is often accelerated quite out of proportion to the amount of pyrexia present, and readings of 130 to 160 are quite common in children (see Fig. 9). The ordinary symptoms of *fever* are, of course, present. Loss of appetite, loss of sleep, indefinite pains all over the body, feelings of chilliness and malaise are all complained of. But three cardinal symptoms stand out prominently, particularly in children. These are sore throat, headache, and vomiting. Young children are not likely to complain so definitely of *headache* as are adults, though no doubt the headache is usually there. On the other hand, *vomiting* is an almost invariable symptom in the young, while it cannot be expected to occur in adults with anything like the same frequency. *Sore throat* is, of course, extremely suggestive, and, even if not complained of by the very young, it is usually sufficiently obvious on inspection. Our older patients, then, will complain of headache and sore throat, and perhaps also vomit. Our youngest ones will almost certainly vomit, and probably by difficulty in swallowing draw attention to their throat. They may also perhaps 'cry with their head', as their mothers say. In children of from five to ten years of age all three symptoms are usually definitely present, and their association is highly important in diagnosis. The feelings of chilliness, commonly complained of, are not infrequently exaggerated enough for the patient to definitely shiver. Well-marked and persistent rigors, however, are not very common. Convulsions occasionally usher in the disease in the

young. Some looseness of the bowels is not infrequently observed, particularly in the sharper cases.

In very severe attacks of a toxic type the vomiting may be persistent, and, as there is often also profuse diarrhœa, the symptoms may suggest irritant poisoning. Delirium may also appear early. On the other hand, in the milder types the rash is sometimes the first obvious symptom, and the invasion period may be said to be altogether missing.

PERIOD OF ADVANCE AND ERUPTION. In describing the course of the fever we will in the first place consider merely the simple type of the disease, and the appearances presented by an average case, excluding for the moment both those which are unusually mild and those which are especially severe. To summarize briefly the main features of the case, the rash appears from three to twenty-four hours after the first symptoms, by which time the temperature has reached, or nearly reached, the level it will maintain as long as the eruption remains bright upon the patient. The throat, sore from the first, becomes markedly congested and often swollen; the glands are frequently enlarged. The tongue, at first covered with thick white fur, rapidly desquamates. If there is much fever the patient's sleep is restless and broken, and delirium is common in children. Adults complain much of headache. After a period, varying from twenty-four hours to four or five days, the rash commences to fade, the throat symptoms to subside, and the temperature to fall by a rapid lysis. If the eruption has been well marked desquamation is visible early. It will be now necessary to examine these features of the disease in detail.

Course of the temperature. There is a considerable difference in the severity and duration of the febrile period in different epidemics, but it may be broadly stated that the fever lasts in the great majority of cases from five to eight days. We have seen that the rise of the temperature is abrupt, usually, indeed, showing as a straight line on the chart (see Figs. 9 and 10). When the acme is reached the temperature remains more or less at the same level during the eruptive period, showing in many cases but little tendency to marked morning remission until the rash begins to fade (Figs. 9, 10, 19). The level attained varies much in different cases, but may be placed roughly between 101° and 104° . Temperatures of 103° to 104° are quite common, and do not necessarily imply that the case is a severe one. The fastigium lasts from one to four days, and is in most instances not more than three. When defervescence begins, which is usually when the rash commences to fade, the temperature relaxes slowly and reaches the normal by three or four morning remissions, swinging up, as a rule, each evening (Figs. 10, 11). Sometimes, however, the brief lysis

does not show this step-like character (Figs. 9, 19), and, in exceptional circumstances, the fall is by crisis (Fig. 18). The complete curve almost reverses that in measles, its abrupt onset, short fastigium, and slow defervescence contrasting with the critical defervescence, short fastigium, and gradual onset seen in the latter fever.

It will be convenient to consider the *pulse* along with the temperature. In the first forty-eight hours it usually remains unduly accelerated, the ordinary ratio to the temperature being frequently much exceeded (Figs. 9,

11). Thereafter it approximates more nearly to the rate which might be expected, except, indeed, in particularly severe cases. It inclines to be small, with moderately high tension. The respirations are not especially accelerated, but maintain their ratio to the height of the temperature.

Appearance of the patient.

The *face*, especially in children, is very characteristic. It is brightly flushed, the colour concentrating itself mainly on the cheeks. The brow sometimes participates in the flush, which is uniform in appearance and shows none of the punctuation characteristic of the rash. The circumoral region, the area surrounding the mouth, stands out pale against the flushed background. This *circumoral*

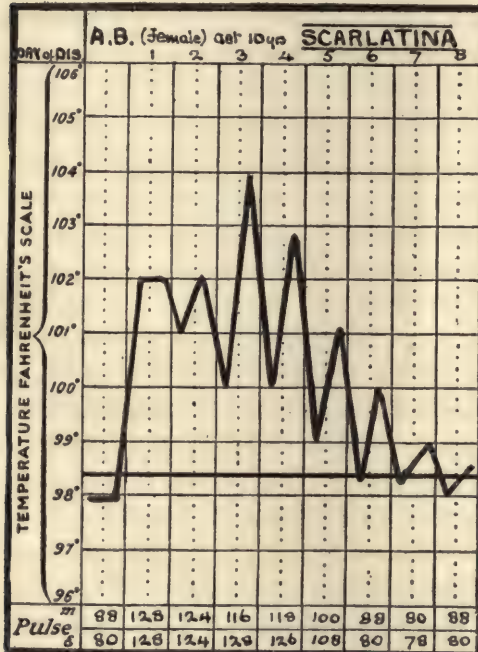


FIG. 10. Case of scarlatina simplex from first day. Note abrupt onset and termination by rapid lysis.

pallor is probably the result of some vasomotor action, and is not merely caused by contrast with the flushed face. The area round the mouth is often quite unnaturally white. The facies, if not pathognomonic of scarlatina, is seldom developed to anything like the same extent in other conditions, but is sometimes well seen in acute lobar pneumonia in children. Adults suffering from scarlatina often fail altogether to present it, though it may be occasionally sufficiently obvious in young women. The *eyes* are usually bright and sparkling, and the conjunctivæ in most instances clear. In more severe cases however, they may be injected, especially for the first few days of the

illness. The *expression*, as a rule, is intelligent, always assuming no delirium is present. It suggests neither the apathy seen in some fevers nor the mental confusion characteristic of others. The features are unaffected, none of the bloating, so often noticed in measles, being evident.

The eruption. The rash of scarlatina makes its first appearance about twenty-four hours from the onset of the disease. When it is delayed longer than forty-eight hours, we may reasonably believe that the original sore throat was due to some other cause than scarlatinal infection. Often

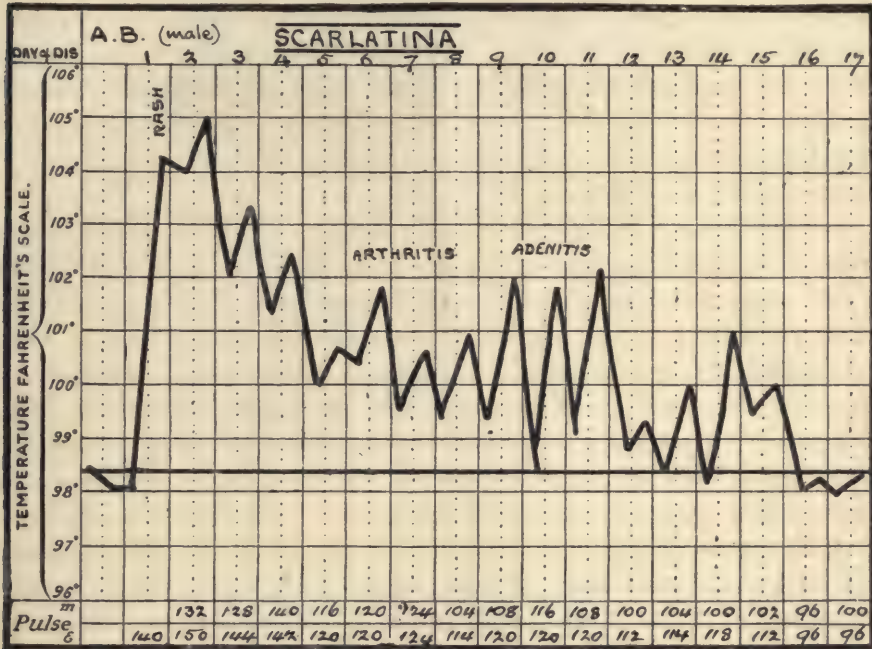


FIG. 11. A sharp case of scarlatina simplex showing lysis interrupted by the appearance of intercurrent complications. Note sudden onset and rapid pulse.

in such cases it will be found that the vomiting occurred some time after the first complaint of sore throat, instead of before it or synchronously with it. The rash appears earliest on the sides of the neck and on the upper parts of the chest. From that situation it spreads downwards over the whole body, last involving the legs. Its development may be extremely rapid, the whole affected surface becoming covered in a few hours, or it may take twenty-four hours or longer before it reaches the legs. When evanescent in character, it may be already fading on the trunk by the time it has fully developed in the lower extremities. In most instances, as it comes out, so

it fades, from above downwards, and traces of it may be sometimes recognizable in the legs, when it has disappeared entirely from the trunk. In well-marked cases it may continue to increase in intensity for two or three days.

In *distribution*, then, the rash may be said to be fairly general, but there are marked exceptions. It does not, strictly speaking, invade the face. We have already seen that the brilliant colour noticed in that situation is merely an intense flush, and that it shows none of the punctuation of the true rash. It may be remarked, however, that the latter trespasses on the face to some extent over the angles of the jaws. In this site well-marked punctuation is not infrequently visible, but it is extremely rare to find any punctate spots on the cheeks themselves. The same applies to the palms and soles, which, often markedly flushed and red, only seldom show definite punctuation, though it must be admitted that the thenar and hypothenar eminences of the hand occasionally are slightly spotted. The backs of the hands and feet, however, participate in the general rash.

As regards the *character* of the rash, it consists of closely set minute points, usually of a brilliant red colour, upon a paler but often flushed background. In mild cases the spots are pink, and the background may appear almost white or yellowish in colour, but as a general rule it is distinctly flushed. The individual punctate spots almost touch each other. They may vary somewhat in size, but on an average will hardly exceed half the diameter of the head of an ordinary pin. Their periphery is not always too clearly defined, often, especially when the eruption is at its height, blending almost imperceptibly with the subjacent erythema. They are not appreciably raised above the surface, that is to say, they cannot be appreciated when the finger is drawn across them. They are obliterated easily by light pressure. The pattern of the hand, firmly pressed on the skin, is left for a few seconds standing out dead white on a brilliantly red background.

In most cases there is some degree of uniformity in the appearance of the eruption, but it is often best marked in certain situations. Thus it is usually very well developed on the back, where its colour is apt to be darker, but where, on the other hand, its punctuation is often not so definitely distinct. The abdomen, again, and the inner sides of the thighs will frequently present a brighter and more definitely punctate eruption than other situations. This tendency of the rash to be brighter in some parts than others occasionally gives an irregular, almost blotchy, appearance to the skin as a whole. As regards the extremities two features of interest are very frequently observed. The punctuation on the forearms and legs is seldom as regular as it is on the trunk. The lesions show a greater tendency to become grouped, and to leave comparatively large areas almost unaffected. The rash, moreover,

PLATE VI



SCARLET FEVER. Note the pallor round the mouth and the fine punctation of the rash.

thus formed is often more papular in character, and is sometimes very distinctly raised above the skin. The arms, then, may present a crude imitation of a measles eruption, the blotchy scattered character of the rash in that disease being in some degree simulated, and the same observation applies to the legs. It must be understood that this blotchy appearance is only seen in a minority of the cases, but it is sufficiently common to demand attention (see Plate IX). The second feature presented by the arms and legs is the great frequency with which, in these situations, the punctate spots are definitely raised, as rough inflamed skin papillæ. It is doubtless a fact that, in many instances, this skin roughness is peculiar to the individual patient, but in any case these inflamed papillæ often retain the colour of the rash, when the latter has altogether faded from other situations.

We have already noted that the *intensity* of the eruption varies considerably. Broadly speaking, the more intense it is the longer it remains visible. It may, indeed, in exceptional circumstances last for over a week, and that without much suggestion of staining or the formation of petechiæ. In extremely brilliant eruptions the very intensity of the process may cause slight hæmorrhage into the punctate spots, and the result is that the skin becomes stained. In such cases the punctate element of the eruption is very clearly seen, and the individual spots admirably defined, especially when the subjacent erythema fades with the onset of defervescence. Sometimes the staining is sufficiently well marked as to be practically petechial, dark purple punctate spots remaining visible for several days after the acute symptoms have subsided. Another result of the intense skin hyperæmia is the formation of a *miliary eruption*, the individual puncta becoming crowned with tiny vesicles containing yellowish fluid, and the whole surface of the trunk, and often of the extremities, is, as it were, peppered by minute yellow spots on a dark red background. The rupture of these vesicles gives us an explanation of the mechanism of scarlatinal desquamation. It leaves a little pinhole breach in the cuticle, and we can well believe that what occurs macroscopically in the miliary eruption, occurs microscopically in the inflamed skin papillæ of the typical rash.

Staining, however, is not limited only to sharp cases. It may be found in certain parts of the body, especially in the flexures of the joints, after a very ordinary rash. In the fold of the elbow, for example, a dark red line is often left transversely across the arm, not fading on pressure, but well stained into the skin. When seen, this is of distinct assistance in diagnosis. Similar lines may be sometimes found at the wrist and knee.

✓ The **throat** invariably shows more or less congestion. The first manifestation of the fever is a well-marked punctation upon the soft palate, which

in many instances will be found to precede the appearance of the eruption on the skin, and may be regarded as the enanthem of the disease. It is best seen in the milder types, as, when there is much throat inflammation, the palate, with the uvula and tonsils, becomes uniformly injected. In many cases the throat lesion is limited to a *congestion*, with slight swelling, of the tonsils; in others the hyperæmia of the palate may be restricted to its free margin and to the uvula. Some stickiness and dryness are often noticed. A further stage in the inflammatory process is well-marked *œdema* of the fauces. The mucous membrane, which in mild cases is merely bright red, becomes darker in colour, and may, if the œdema is intense, assume a purplish, plum-coloured appearance. The tonsils almost meet, and are sometimes enormously swollen, and much sticky mucus clings to their inner surface. The voice becomes thick and choked, swallowing is extremely painful and difficult, and, in rare instances, the breathing may be seriously obstructed, though very seldom sufficiently so as to require relief by operation. On the other hand, the intensity of the inflammation may be considerably less, and the œdema only moderate, but *patching* may appear on the inner surface of the tonsils. A yellowish scum, usually quite easily detached, patches the mucous membrane and clings to the crypts. Its removal leads to no bleeding and leaves no obvious abrasion or ulcer, but it is extremely apt to recur. This patching is practically invariably limited to the tonsils. It may form a continuous pellicle, or appear as separate areas of exudation. A further stage in the inflammatory process is *ulceration*, often starting under patches such as those already described, owing to a superficial necrosis of the mucous membrane in that situation. If the ulceration is well marked, it is usually not restricted to the tonsils, but may invade the pillars of the fauces and even the palate itself. It is, however, only serious in cases of septic scarlatina, and it will be further considered when that type of the fever is discussed.

The tongue. A careful study of the tongue in scarlatina will be found of great assistance when doubtful cases come under notice. It is reasonable to assume that the same hyperæmia and inflammatory action which are concerned in the production of the punctate eruption with its congested skin papillæ cause similar changes to occur on the surface of the tongue, and especially affect the papillæ of that organ. The appearances observed succeed each other in regular gradation, and, as a rule, can be predicted with confidence. For purposes of convenience we will describe them as seen on each succeeding day of the disease in an average simple case, it being thoroughly understood that in some patients the changes occur somewhat more rapidly than in others. On the *first day*, then, thick white creamy fur



THE PUNCTATE RASH OF SCARLET FEVER.

rapidly accumulates on the tongue, until by twenty-four hours the whole organ is thickly plastered with white. This collection of fur, by no means pathognomonic of scarlatina, is due to an excessive proliferation of epithelium. During the *second day* swollen, red, prominent papillæ begin to protrude through the fur, and the general appearance given is that of numerous red dots on a white creamy surface. This tongue, called by some the 'white strawberry' tongue, may be met with in other diseases than scarlatina, and indeed is frequently seen in diphtheria and measles, but in these latter conditions the fungiform papillæ will not be found so prominent or so large, if examined closely. Even on the second day the desquamation of the fur has usually commenced, the tip and edges of the tongue being often clean and of a vivid red colour. On the *third day* the desquamative process has still further advanced, the fur frequently peeling off in strips from before backwards, leaving what may be called a 'transition' tongue, presenting in different areas the features of both the red and the white strawberry types. By the *fourth day* it is usual to find that the last traces of fur have disappeared, except perhaps from the extreme back of the organ. The tongue is now the characteristic tongue of scarlatina, the so-called 'red strawberry'. The colour is a deep red, and the papillæ all over the surface are prominent and often œdematous. The fungiform papillæ are especially well marked, and the back of the tongue, particularly, is very rough. The terms 'strawberry' or 'raspberry' are hardly misnomers. They express fairly accurately the appearances presented. During the few succeeding days the tongue remains clean, but the papillæ gradually subside and the colour by degrees becomes paler. When there is much glazing, as observed chiefly in patients who sleep with their mouths open, the tongue has been aptly compared to 'raw beef', which, indeed, it very closely resembles.

In mild and moderate cases the changes may not be always so obvious as above described, and again in very sharp cases the tongue often cleans rapidly, the fur having entirely disappeared by the third day. Sometimes, again, the 'third day' appearance of a partially denuded tongue may be seen as late as the fourth or even the fifth. But I find that in probably five cases out of six, or more, it is possible from the appearance of the tongue alone to guess accurately how long the patient has been ill, and that an estimate is almost never more than a day wrong. This definite course of the desquamation is of great value in diagnosis, as, if the appearances of the tongue correspond fairly accurately with the history of the illness, the presence of a rash is not required to make the fever recognizable. A point worth noting is that the 'red strawberry' tongue, as well as being a practically invariable phenomenon of the fourth day, is also characteristic of the

subsequent days of the fever and is often diagnostic, in its gradually modifying form, as late as the seventh, or even the ninth, day of illness. By that time, however, the normal fur of the tongue has, in most cases, begun to lightly coat the surface.

During the height of the fever the skin is extremely hot to the touch, and its peculiar pungency has been stated to be characteristic of the disease. A very intense rash sometimes causes irritation, and makes the patient restless and uncomfortable. The skin is dry throughout.

The **glands** in the acute stage of the illness are usually more or less enlarged, and the amount of swelling which they present is roughly in proportion to the severity of the throat. The glands affected are principally those lying below the angle of the jaw, but slight enlargement and even tenderness may be appreciated in even the posterior cervical group in many cases. This is of some importance to remember, as, in mild cases of scarlatina, the affection of the glands in this situation might lead to a diagnosis of rubella. These glands are, however, easily palpable in so many presumably normal children that their association with many cases of scarlatina may be merely accidental. Severe glandular swelling is invariable in the septic type of the fever, to the consideration of which the reader is referred.

Nervous symptoms are not particularly prominent in simple scarlatina. We have seen that the attack may commence with convulsions in young children. Headache may persist throughout the febrile period and some adults appear to suffer much from it. When the temperature is high, sleeplessness is a common feature and may require treatment. In more moderate cases the sleep is restless and often broken, but, as a general rule, the patient obtains a sufficiency of it. Delirium is chiefly seen at night. Occasionally it is of the excited variety, the patient attempting to get out of bed. More usually it is manifested merely by confusion of ideas and the talking of nonsense. It is most rare for a case of scarlatina simplex to present the symptoms of the typhoid state; and even those who suffer from delirium at night are fairly sensible during the day. The nervous symptoms are much exaggerated in toxic cases, and also in the septic variety of the disease.

The *digestive system* is always more or less upset. The appetite is lost, and in young children thirst is a prominent symptom. Though the bowels are not infrequently loose at the onset of the illness, constipation is the rule during the eruptive period. Vomiting occasionally persists for a day or two, even in mild cases, but possibly it is due to nervous rather than to gastric causes.

The *urine* in the febrile stage is scanty and high coloured. Caiger notes

that at first the amount of urea excreted is in proportion to the height of the temperature, and that with a temperature of 103° it may be as much as 4 per cent. Later on this relation is lost, and the amount of urea falls from the fourth day. When the temperature regains the normal, large quantities of pale urine are usually passed. In patients with high temperature albuminuria is not uncommon, and need not be regarded seriously. Although Klein has described interstitial changes in the kidney as occurring in the first few days of the illness, it is doubtful if the organ suffers more in this stage of scarlatina than is common in other acute febrile conditions, and clinical experience is against the assumption that this early albuminuria has any relationship to the true nephritis of convalescence. In sharp cases, and above all in those which have any suggestion of septicity, the diazo reaction is present throughout the eruptive period. Lauder Thomson, who investigated this point at the City Hospital, came to the conclusion that the presence of the reaction implies that a case will be more than averagely severe. It is unusual to find it present in mild cases.

The **blood** usually presents a well-marked leucocytosis. Bowie, who has made a most exhaustive study of this question, holds that this increase in the number of white corpuscles usually begins during the period of incubation. It reaches its maximum at, or shortly after, the height of the severity of the disease. The more severe the case, the higher is the leucocytosis and the longer it lasts. In serious cases a high count is of more favourable import than a relatively low one. The increase in the white corpuscles depends upon an absolute and relative increase in the number of polymorph cells. Eosinophiles are diminished at the onset of the fever, but increase rapidly afterwards and occur in such a comparatively high percentage that, according to Bowie, a differential count might assist in diagnosis from other conditions. This high percentage may be maintained for some days after the end of the first week even in mild cases. The count in simple scarlatina appears to range from 7,000 to 34,000 during the febrile period. In septic cases it is considerably higher, varying from about 14,000 to 40,000 cells. The main points of practical value seem to be, first, the possibility of suspecting the existence of the disease in an exposed person by finding a leucocytosis during a possible incubation period; second, the diagnostic value of well-marked eosinophilia on about the fourth or fifth day of a doubtful case; and third, the fact that, in a case with very severe symptoms, a comparatively low count is a bad prognostic sign.

Dudgeon notes that the blood in bad cases is very fluid and coagulates slowly. He considers that this feature, although seen in other severe inflammatory affections, is especially well marked in scarlatina, and the

way the blood flows, when a prick is made for a count, indicates to some extent the nature of the attack.

A great amount of attention has recently been given to the so-called 'inclusion bodies' first described by Döhle. These are usually round or oval grains in the protoplasm of the polymorph cells, but occasionally other shapes such as rod-like bodies, spiral threads, and pointed forms are observed. They take on basic dyes, staining a little more faintly than the nucleus, and can be well demonstrated by the use of carbol methyl blue. They have no connexion with the nucleus, and can be, indeed, differentiated from it by special stains, and have been regarded by some observers as a kind of concentration of protoplasm. A variable number of the leucocytes contain the inclusions, and the numbers in each vary, usually one or two being present. Döhle's suggestion that they are concerned in the etiology of the fever has not found support among the many workers in this field, but a certain number, notably Kolmer and Nicoll, consider them to be of real diagnostic value. They occur, however, fairly regularly in the blood of diphtheria patients, in erysipelas and other streptococcal and septic infections, and, according to the majority of writers on the subject, also in measles, although Nicoll states that the granules in measles are smaller and not absolutely identical with those observed in scarlet fever. Practically all agree, however, that they are present in nearly every case of scarlet fever up to the fourth or fifth day of illness, and that their absence therefore may almost be said to exclude that disease. Nevertheless Granger and Pole found them absent in the fatal toxic type of the fever, and Nicoll and others admit they are occasionally wanting in very mild types. They are not present in serum rashes which occur at some interval from the acute diphtheria attack, and this fact might be of assistance in making what is often a very delicate distinction. We may conclude that in the meantime at any rate it is impossible to diagnose scarlet fever by film examinations alone, and that therefore the method is hardly a suitable one for the reporting laboratory, although it appears to be made use of to some extent in the United States.

Stage of defervescence and commencement of desquamation.

With the gradual fall of the temperature, already described, the patient's symptoms rapidly improve. The rash, as a rule, fades synchronously with the commencement of defervescence. The throat becomes quickly more comfortable, unless, indeed, it remains patched, in which case the fall of the temperature may be delayed or incomplete.

In well-marked cases, however, desquamation is visible before the defervescence begins. Apart from its first manifestation, the peeling of the

PLATE VIII.



Early desquamation showing as white points on the skin of a patient whose rash has not as yet entirely faded. Here and there small circular pinholes may be seen.

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tongue, it is often recognizable on the cheeks by the third or fourth day of the illness. In this situation it appears as a very fine powdering, sometimes sufficiently marked to give what Caiger has happily termed the 'powder and rouge' appearance to the face, the brightly flushed cheeks being toned down, as it were, by the fine white powder. In less marked examples of the fever this early skinning is not always visible, and the first evidences of desquamation are likely to be found on the lobes of the ears and the sides of the neck. In character the appearances vary considerably. In some cases there is, merely, an almost impalpable powdering, and the shedding of the cuticle may be only appreciated when the patient is being rubbed down after a bath. This is particularly the case with infants, who may be said, as a general rule, to powder rather than peel. In most older children, however, the process of desquamation is fairly evident. It has already been mentioned that in the miliary eruption, sometimes seen in the fever, we can follow the mechanism by which, we may assume, the process usually occurs. The summit of an inflamed skin papilla ruptures, and a small breach in the skin is left, which, increasing in size, is soon visible as a 'pinhole' in the cuticle. By the further increase in the size of these minute breaches in the epithelium, and by their coalescence with each other, flakes of skin of a larger or smaller size are detached. This form of desquamation is best seen on the neck, chest, and outer surfaces of the arms, forearms, and thighs. The skin of the legs, usually more rough, often powders coarsely and is less liable to show a pinhole arrangement.

Desquamation occurs in the following sequence. The face commences to powder during the febrile period, and by about the seventh day in an average case the ears, neck, and upper part of the chest show evidence of skinning. From these situations the process extends downwards over the trunk and arms. The hands begin to show broken epidermis about a fortnight from the first symptom. Occasionally, however, the skin in this situation may not commence to peel until towards the end of the third week. The first sign on the hands is, often, splitting of the skin in a line with the free edge of the nail. The hard skin of the palm is detached in tough flakes and is sometimes even shed *en masse*, it being occasionally possible to obtain almost perfect gloves of skin. Peeling between the fingers in a doubtful case is of more value than desquamation on the palm, as the latter is sometimes merely the result of a hand, accustomed to manual labour, being rested for two or three weeks, and it is usual for labourers to desquamate in this situation after any acute illness. The toes begin to split shortly after the fingers. In an ordinary case the skin should be found broken about three weeks from the onset of the fever, though sometimes it may be a little later.

By the end of four weeks desquamation is usually completed except for the palms and soles, and the former seldom show any skinning after the fifth week is over. It may be many weeks more before the tough epidermis has separated from the sole, particularly at the heel. Even in this situation, however, the skin has often become detached by the end of the sixth week, and it is only in persons with extremely hard feet that the completion of the process takes longer than eight weeks. We must, on the other hand, be prepared to occasionally find the old skin still adhering, even when ten or twelve weeks have elapsed. We have already noted that this late desquamation need not be regarded seriously.

To sum up, then, it may be said that desquamation is usually evident by the end of the first week, that the trunk and extremities have finished peeling or powdering by the end of the fourth, and that any subsequent skinning is limited to the palms and soles. In diagnosis it may be important to compare the situation of any supposed scarlatinal desquamation with the time which has elapsed since any attack of sore throat, sickness, or erythema from which, it may be alleged, the patient has suffered.

Occasionally a secondary desquamation may take place, another layer of the cuticle being shed. It may be added that, broadly speaking, the desquamation is rapid and well marked in direct proportion to the intensity of the eruption. In a miliary case, for instance, the whole body, except the hands and feet, may be free from desquamation within the fortnight. On the other hand, very mild cases, the diagnosis of which may have been doubtful, may have to be kept under observation for three weeks before definite peeling on the hands shows their true nature, no desquamation having been visible on the trunk and extremities.

TYPES OF SCARLATINA. Mild forms. The form already described as average scarlatina, the type known as scarlatina simplex, is, except for its possible complications in convalescence, always benign, and therefore might be included under this heading. But it is quite common to meet with cases in which the symptoms are so trivial that it is hard to believe the disease is, in reality, scarlatina. The eruption in some instances may be extremely transient, lasting only for a few hours, and perhaps limited to the upper part of the chest. The other symptoms of the illness may be either reasonably well marked or only slightly developed. These cases are very apt to be missed, and may not be recognized until definite desquamation occurs. Other patients may present an excellent and even brilliant rash, and yet have no fever at all. I have seen even completely apyrexial cases. Usually, however, the temperature is slightly elevated, as in Fig. 12, although the pyrexia may be only initial and subside some days

before the rash has disappeared. It will be noticed in this chart that not only did the rash remain visible for five days, but that the pulse in the first twenty-four hours was distinctly rapid. The patient, in fact, was much more ill than the pyrexia suggests. But often, when the fever is so slight, the rash is evanescent, the throat only moderately injected, and there is no obvious malaise. Such cases may readily escape recognition, and it is well in school or house outbreaks to regard even a simple sore throat as suspicious.

Severe forms. It is to these types that the mortality of scarlatina is due. They may be classed as either *toxic* or *septic*. Under the first of these headings are included patients who are, as it were, overwhelmed by the toxins of the disease itself, without any exceptional local manifestations or complications. In the second group fall those cases in which a septic local condition appears to cause a general septicæmia.

Toxic scarlatina, usually termed *scarlatina maligna*, is nowadays comparatively rare. It varies much in its frequency in different localities and epidemics, but only once in the last twenty years have toxic cases been more than 1 per cent. of the total admissions to the Edinburgh City

Hospital, and of late years they have been exceedingly rare. With the exception of three or four all terminated fatally on or before, usually indeed much before, the fifth day of illness. This fatal type of the disease may be due either to an excessive dose of a virulent infection, or may be the result of an ordinary dose being met by only an unusually low resistive power. That the latter may occasionally be the case is indicated by the fact that members of a particular family will succumb to this form of the fever, although they contract the illness at different periods and during different

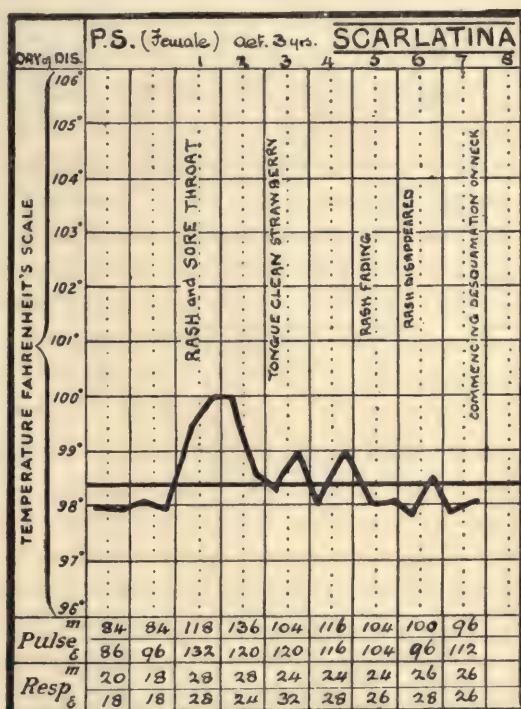


FIG. 12. A mild case of scarlatina. Subacute temperature for first two days, thereafter normal temperature with visible rash.

epidemics. The main characteristics of the toxic type may be summed up as very severe general symptoms, associated with only moderate faucial lesions, and progressing to an early fatal termination. There are various subtypes, which, however, depend chiefly on slight differences in the degree of the virulence of the poison, or of the resistance of the person attacked, and on the vulnerability of the various tissues involved. These varieties are not well defined, and are difficult of exact classification, but many patients will fall naturally into one of the three groups mentioned below, it being clearly understood that gradations between the groups are frequently noticed.

Fulminant type. This form of the fever is the real 'scarlatina maligna'. Its course is so brief, and the difficulty of immediate diagnosis often so great, that the patient seldom lives to reach hospital. It is also, fortunately, extremely rare. The patient, previously perfectly well, is suddenly struck down. Intense headache, and often rigors, may commence the attack, but the most prominent symptoms are probably persistent vomiting and profuse diarrhoea. These latter features may be so accentuated as to arouse a suspicion in the mind of the medical attendant that the patient is the victim of irritant poisoning. The temperature is high at first and may attain hyperpyretic levels, but, towards the end, the patient is in such a state of collapse that it may fall to normal or below. Some degree of sore throat is usually complained of, but in spite of the violence of the general symptoms the fauces may be only slightly congested. Delirium, to a greater or less degree, is often present. As regards the eruption, the case often terminates so rapidly that it cannot be reasonably expected to appear. Should, however, any be present, it is badly developed, scattered, and dusky in appearance. Death is seldom delayed for more than twenty-four hours. Baginsky states that it may even occur in a few minutes, but such extraordinary rapidity of course must be exceptional. Perhaps from twelve to twenty-four hours would be the average duration of such a case. It is obvious that diagnosis in these circumstances depends chiefly on the knowledge that the patient has been exposed to the infection, and on the presence of other cases in the family. When suspected, any suggestion of a rash, taken together with the throat and vomiting, will help its recognition.

Ataxic scarlatina. This form presents the features mentioned above, only in a less degree. The patient usually survives from two to four days. The throat is often obvious, but seldom severe. It is unusual for it, in my experience, even to be slightly patched, but it is occasionally considerably swollen and dark in colour. The eruption develops badly. It may appear late, or only be coaxed out by continual applications to the skin, or by hot

baths. It is dusky in colour, often scanty, or limited entirely to the trunk and back, and disappears imperfectly, or not at all, on pressure. It may be somewhat blotchy in appearance, owing to its irregular distribution and varying intensity in different situations. Sometimes it is more erythematous than truly punctate. The temperature is high, and seldom is below 105° even from the first. It has a tendency to run to hyperpyretic levels and can seldom be effectually controlled, death being usually preceded by a rise to anything from 108° to 110° . The pulse is always rapid, usually 160 or 170 in adults, and sometimes uncountable in children. Nervous symptoms are a prominent feature. Convulsions may be repeated at comparatively short intervals in young children. Marked insomnia, delirium, picking at the bedclothes, and subsultus of the tendons are commonly observed. Headache is often extremely severe, and vomiting is in some cases almost persistent. Diarrhœa, though frequent enough, is not invariable, but some looseness of the bowels is usually present. Before the end comes it is quite usual to see a general lividity of the skin, particularly on the trunk, which may be stained a deep purple.

Adynamic scarlatina has many features in common with the above, but its main feature is that the heart and circulation appear to suffer more than the nervous system. The throat is only moderately affected. The temperature is usually not especially high, perhaps varying from 103° to 104° , or even lower, till just before the fatal termination. The pulse is rapid and is much softer than is usually observed in ataxic scarlatina. The face is often extremely pale. The rash is often well enough developed, but is very dark and sometimes petechial. Both vomiting and diarrhœa may be present. Delirium and marked nervous symptoms are not well marked, and the patient is neither restless nor excited. His weakness, indeed, keeps him more or less quiet. In many of these cases the initial symptoms are not unduly severe. It appears to be the gradually failing heart which converts

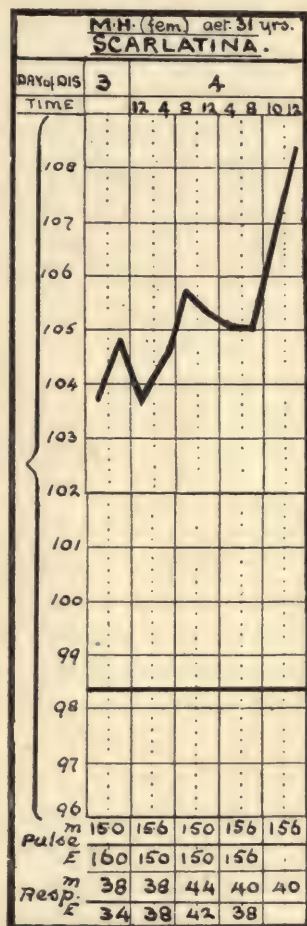


FIG. 13. Toxic scarlatina.
Death on fourth day.

what has seemed merely a sharp simple case into the toxic type. Death occurs most frequently on the fourth or fifth day, seldom earlier.

The possibility of an apparently simple case becoming obviously toxic must not be forgotten. Usually, in my experience, such cases assume the adynamic type, but I have seen patients who were only moderately ill at the outset develop marked nervous symptoms and hyperpyrexia on the third or fourth day. The rash, which may be well out, becomes petechial, the individual punctate spots being stained deeply.

A hæmorrhagic form of scarlatina maligna has been described, with hæmorrhages from the mucous membranes and into the skin. Such a case has never come under my notice, and it has been suggested that some, at least, of those reported were instances of hæmorrhagic small-pox, which frequently presents a scarlet initial rash.

I have always been accustomed to limit the term 'toxic' to those which may fairly be considered 'malignant'. The word is sometimes used a little loosely of patients who are, in reality, septic. No doubt the germs responsible for septic infection have toxins of their own which must play a large part in ultimately producing a fatal result, but, as Foord Caiger has suggested, it is well to restrict the term 'toxic' to those cases which show evidence of poisoning by the toxins of the scarlatina organism itself, whatever that germ may be. It may, of course, be sometimes impossible to draw a definite line between the toxic type and instances of very severe simplex. Perhaps the safest way is to decline to recognize recovery as compatible with a genuine toxic case, but on two or three occasions I have seen what I believed to be a real one recover.

Septic scarlatina. Very different in its course and manifestations is the septic variety, the type commonly spoken of as *scarlatina anginosa*. In this form of the illness the main cause of the severity is the septic and often putrid condition of the throat. This is patched from the first, is much swollen, and rapidly becomes ulcerated, superficial necrosis occurring on the tonsils and gradually involving other structures. The glands are much enlarged from the onset. The rash is usually well developed, and often intense, but shows a tendency to be somewhat irregular and blotchy in character, particularly on the extremities. But, when it commences to fade, there is no amelioration in the other symptoms. The temperature, usually high from the first, remains elevated. The rapid pulse-rate is still maintained. The nasopharynx becomes involved in the inflammatory process, if, indeed, this has not been obvious from the onset, and purulent discharge sometimes literally pours from the nostrils. At first, however, the discharge is thin and watery, and apparently intensely

acid in character, causing much redness and soreness at the orifices of the nostrils and on the upper lip. This discharge, moreover, is frequently inoculated by the nails of the patient into the skin of the face in other situations, and a pustular eczematous eruption may appear in consequence. The cervical and submaxillary glands continue to increase in size, and, in some cases, by meeting below the chin surround the neck with a collar of infiltrated glandular tissue very hard to the touch, and sometimes extending from the lower jaw to the clavicles.

With such severe local conditions the patient, usually a young child, is obviously very ill. He suffers much from pain in swallowing, from the soreness of the nose, and from the general discomfort caused by his fever. Delirium is commonly present at night. At all times the sufferer is restless, irritable, and resistive. Septic scarlatina, indeed, makes the worst-tempered patients in my experience. A diphtheria child submits readily to local treatment within twenty-four hours of admission; the patient with scarlatina anginosa struggles to the end. No doubt throat and nose treatment in these cases is extremely painful, but none the less the child is unduly irritable, and never learns that it suffers less by resigning itself.

During the second week the temperature is often irregular, sometimes showing great variations. Its course is influenced by the onset of the different complications, which now begin to appear. Arthritis is fairly common in such cases, and in most instances there is double otitis media. It is easy to see how the ear becomes affected, when the condition of the nasopharynx is considered. Broncho-pneumonia not infrequently supervenes, and may sometimes be due to particles of food entering the respiratory passages, owing to the great difficulty in swallowing. About this time, also, septic rashes of a very angry red character are apt to make their appearance. They are often limited to the neighbourhood of the joints, especially the elbows and knees, and are blotchy and sometimes almost measly in character. The suggestion of measles, indeed, is sometimes very marked, as occasionally such a rash may be more widely spread, and even invade the face. These rashes often become stained into the skin.

In a certain number of patients improvement is noted about the commencement of the third week, but it is quite usual for a case of this type to run for three or four weeks and terminate fatally, as illustrated in the chart (Fig. 14). In such prolonged fevers the condition of the throat, in spite of the greatest care, often becomes horrible. The soft palate may ulcerate away from its edge, until but little of it remains. The uvula may be destroyed. Perforations of the pillars of the fauces,

or of the soft palate, are not infrequently observed. Goodall suggests that the organisms of Vincent (see Plate XXIII) may be sometimes responsible for such ulceration, but they are by no means invariably present. I have, however, seen them associated with palatal ulceration on one or two occasions. Stomatitis, to a greater or less degree, is present in nearly all septic cases which are at all prolonged.

The patient is much wasted, partly on account of the prolonged continuance of the fever, partly, no doubt, because of the great difficulty in giving him sufficient nourishment. Towards the end diarrhoea is often present, and albuminuria common. In my experience, however, hæma-

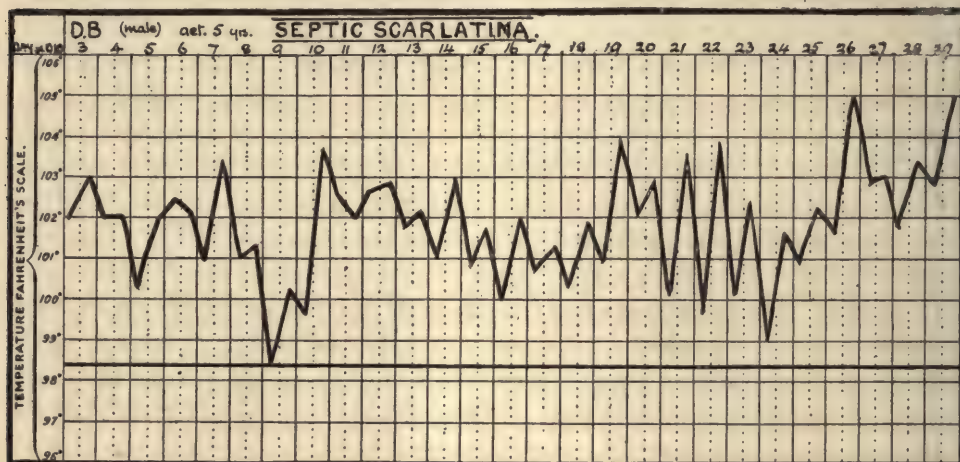


FIG. 14. Showing temperature curve in a case of septic scarlatina fatal on the twenty-ninth day.

turia is rare. The pulse becomes extremely rapid, the respirations are accelerated as the result of pulmonary congestion or broncho-pneumonia, and the patient finally succumbs, the temperature often running up before death. In favourable cases convalescence is slow and interrupted by accesses of fever, due to the condition of the ears or to suppuration in the glands.

It is unusual for older children or adults to run a typically septic course. The worst cases seem to occur in children of about six years of age and under.

The typhoid type of scarlatina. My experience of this variety of the illness is that it is rather a prolonged, than a particularly severe, type. It is of course the case that certain truly 'toxic' patients drift into the 'typhoid state' before they die, but in their case the presence

of enteric fever is not suggested either by their appearance or symptoms. In the type under consideration, however, the outstanding feature is the resemblance of the general course of the disease to that fever. The patient suffers from a well-marked, and often distinctly sharp, attack of scarlatina, but his general symptoms do not subside with the disappearance of the eruption. The temperature, on the contrary, remains up and assumes a more or less remittent type (see Fig. 15). The throat regains the normal and there is a complete absence of local lesions to account for the pyrexia.

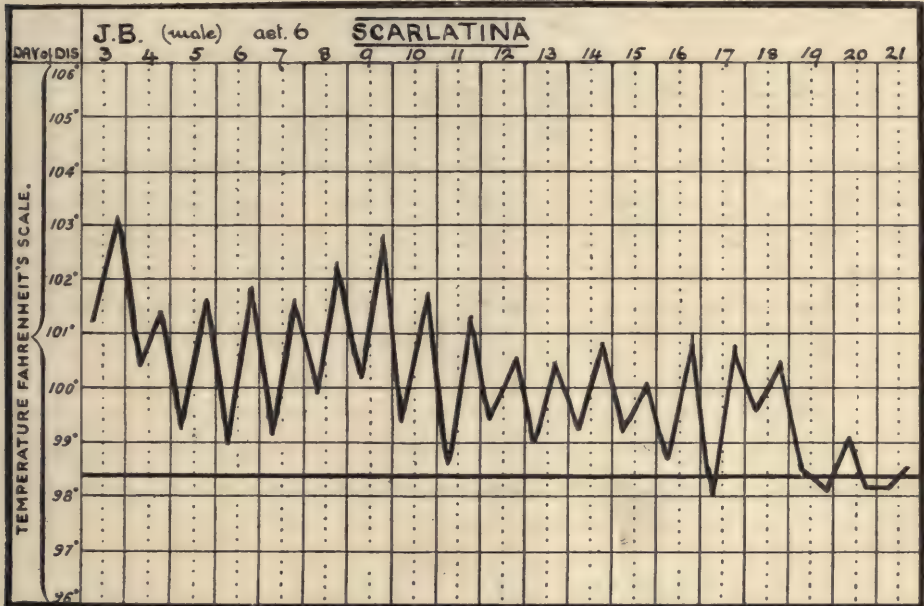


FIG. 15. Illustrating scarlatina of the typhoid type. In this case the throat was merely congested and there were no septic symptoms.

The pulse is, as a rule, moderate. In appearance the patient much resembles a case of enteric fever, and this, taken together with the course of his temperature, causes considerable difficulty in diagnosis. The spleen, moreover, may be appreciably enlarged. In the cases which I have observed looseness of the bowels has not been common. The patient may succumb to exhaustion, but, so far as my very limited experience of this type goes, usually recovers. Should death occur, the Peyer's patches are found enlarged, but never ulcerated.

I have not seen many more than a dozen instances of this type of scarlatina. In most of them it required several negative serum tests to dismiss the idea that they might be enteric fever. It must not, of course, be

forgotten that the two diseases may run concurrently. I have seen three instances of this concurrence and remember one case in which typical typhoid spots appeared on the abdomen in the midst of a scarlatina rash which was just beginning to fade. In that patient both illnesses ran a perfectly normal and quite typical course. But the typhoid type of scarlatina depends on some quite different infection, possibly, as Goodall suggests, septic in nature.

Surgical scarlatina. By this is understood scarlatina occurring in patients recently operated on, or treated in surgical wards for such an injury, for instance, as a burn. The identity of some of these cases, which are usually characterized by their mildness, with true scarlatina has been questioned, but there can be little doubt that many of them are, in reality, instances of that disease. The possibility, however, of a septic erythema, particularly in connexion with a burn, must not be lost sight of. It has been unusual, nevertheless, for patients admitted to the City Hospital with scarlatiniform rashes, following a surgical lesion, to contract the disease, and desquamation has, as a rule, been characteristic enough. It is not necessary to assume that the point of entrance of the virus is through the breach in the skin. The naturally depressed condition of such a patient might well predispose him to infection by ordinary channels, and similar mild forms are sometimes observed in patients treated in medical wards. It must be remembered that some surgical patients contract the disease in an averagely severe, or even dangerous form, and too much stress must not be laid on the usually benign course of such cases.

There is, I think, reason to believe that *traumatic infection* with the scarlatina virus is perfectly possible. I have seen a case almost exactly similar to the classical one of Von Leube. A house-surgeon at the Edinburgh Royal Infirmary pricked his finger when opening a suppurating gland in the outpatient room. When I saw him three days later a bright scarlet punctate rash covered the affected arm and was spreading over the chest. Through the rash the lines of inflamed lymphatics were clearly visible. His throat at this time was only just commencing to be painful, but he had vomited some hours earlier. Next day he presented a general rash and all the typical signs of scarlatina, the throat and tongue and subsequent desquamation presenting no differences from an ordinary case. The patient on whom he had operated commenced desquamating on the hands shortly afterwards, and was admitted to the City Hospital. It is, of course, possible that he contracted his illness in the ordinary manner, but the unusual course of the eruption certainly suggested that the origin of the fever was traumatic.

Puerperal scarlatina. *Pregnant women* are not very frequently affected by scarlet fever, but a considerable number have come under my notice in the last twenty years. The disease has not been severe, and I do not remember seeing an instance of abortion, scarlet fever differing very much from measles and small-pox in this particular. Several women, however, have been confined at full time while in hospital and both mothers and children did well, the only fatality occurring in a case alluded to below. It has been held that, in the *puerperium*, women are peculiarly liable to infection, and that puerperal fever often results. This view is, I think, erroneous, and is probably based on the frequency with which rashes of a scarlatiniform type complicate cases of puerperal sepsis. Goodall, who has given special attention to this question, holds 'that a woman who has been recently confined is no more likely to contract scarlatina than any other woman who is not quite in her normal health; and, if she does, the attack is not necessarily severe'. As regards the latter point, Foord Caiger, on the other hand, regards the occurrence of scarlatina in the puerperium with great apprehension. It is of course obvious that the lacerated condition of the genital organs opens the way to infection from the discharges of the nose and throat, and a condition analogous to septic scarlatina might well result, if great care is not taken as regards antiseptic precautions, and anxiety is certainly well founded, but, on the whole, my experience of about a dozen of these cases has been reassuring. Of the last five under my care four recovered with no evidence of sepsis and the fifth died of a toxic attack on the fourth day of illness, the fifth day after her confinement, but manifested no septic symptoms. Another fatal case delivered of a dead full-time foetus on the second day of her fever, by which time the throat was already in a septic condition, died as the results of both puerperal infection and scarlatina anginosa. In this case the woman had fully developed scarlet fever before her delivery. Whether the practitioner is always justified in attending both confinements and patients with scarlatina at the same time may be reasonably questioned, but, if no substitute is available, as must often be the case in country practice, he can probably do so perfectly safely, provided he exercises scrupulous care in the disinfection of himself and his belongings.

RELAPSES AND SECOND ATTACKS. Relapse in scarlatina, though not extremely common, is a well-established phenomenon, and occurs much more frequently than many senior practitioners seem inclined to believe. It is not, moreover, as Boddie and others have shown, limited to hospital practice, and must therefore in some instances be due to auto-infection as is the case in enteric fever. It consists of a repetition of the

original fever, in most cases in a considerably milder form. This, however, is not always the case, and Foord Caiger holds that the severity of a relapse is in inverse ratio to that of the original attack. I have never seen a relapse terminate fatally, and even sharp attacks have been in my experience unusual. Perhaps the most frequent time for one to occur is in the fourth or fifth week of the illness, especially the former, but its appearance may be delayed until the sixth or seventh week. I do not remember seeing an earlier example than the one illustrated in the chart (Fig. 16). Sore throat and the usual symptoms of invasion and eruption are present in the relapse,

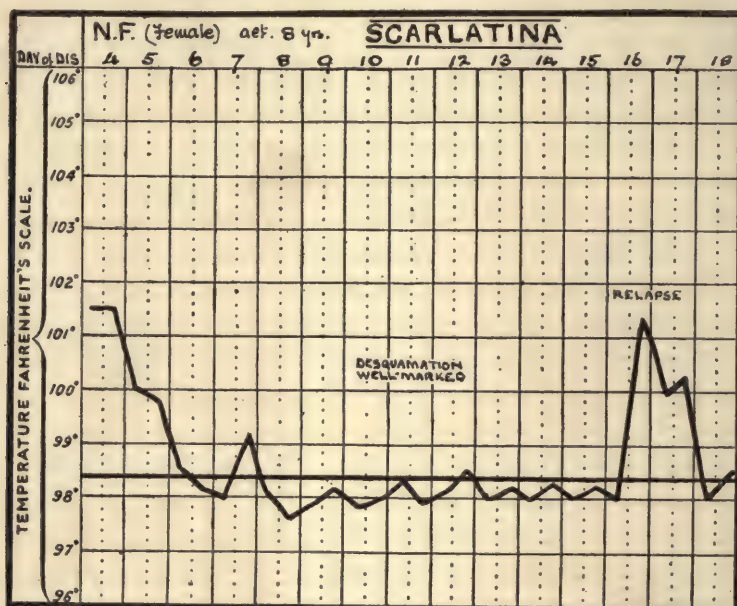


FIG. 16. A moderately severe case of simple scarlatina.

and desquamation follows in due course. There is nothing, indeed, to distinguish the condition from an ordinary attack of scarlatina. In Edinburgh relapses occur in considerably less than 1 per cent. of the cases, and this experience coincides with that of other fever hospitals.

Second attacks of the fever not infrequently occur, but only as a rule after a considerable number of years. Nevertheless, in my twenty years' work at the City Hospital I have treated several individuals in two attacks of scarlatina, both perfectly genuine and typical.

COMPLICATIONS. During the period of desquamation certain complications are extremely liable to occur, some showing a preference for a particular stage of convalescence, others appearing indifferently at almost

any time during the patient's isolation. Schick has made a distinction between the group of complications which often occur early and appear directly associated with the original fever, such as arthritis and primary adenitis, and the group which does not appear until a distinct interval has elapsed, as for example nephritis and late adenitis. To explain the latter he adapts the theory propounded by von Pirquet and himself to account for serum sickness and the acute eruptive stage of measles, small-pox, and chicken-pox. He considers the incubation period of scarlet fever too short and too variable for its acute eruptive symptoms to be accounted for by the anaphylactic phenomenon, but he regards the fairly definite time limits within which nephritis and late adenitis commonly arise as pointing to these complications, at least, appearing in consequence of some anaphylactic reaction. The original infecting substance, the unknown germ of scarlet fever, in addition to causing the original symptoms of the illness, a task in which it is assisted by the streptococcus, causes the development of reaction bodies after a fairly definite interval, just as the development of similar bodies is caused by the injection of a foreign protein. With the development of these reaction-bodies, or ergins, a period of specific hypersensitiveness commences and, while it lasts, latent germs remaining over from the primary attack may succeed in becoming active. If no germs remain latent there are no sequelæ, and it may be assumed that symptoms depend on the amount of germs, the degree of hypersensitiveness, and the presence or absence of exciting causes. While it may be admitted that such auto-reinfections can occur in scarlet fever, as indeed is evidenced by the occurrence of relapses, a suggestion put forward by Cederberg seems worthy of notice. He assumes that the protective mechanism of the body tries to free itself of the infecting germs, and often succeeds in doing so before the appearance of the ergins in the blood, in which case no sequelæ occur. But if the germs, which are presumably excreted by the kidneys, are caught, as it were, in that organ by the sudden appearance of ergins in the circulation, their interaction produces locally a toxic substance which is responsible for the nephritis, and the glands may also suffer if they have not become free of germs.

Nephritis, while by no means the most common complication, is perhaps the most important and interesting. It is usual in statistics to class late *albuminuria* and true nephritis separately, but it is very difficult to draw any definite line between them. It is not unusual to find tube casts in cases of very slight and transient albuminuria, and the complication tends to occur at the very period of convalescence at which acute nephritis, with hæmaturia and well-marked symptoms, is most apt to

present itself. It is hard to resist the conclusion that the difference between the two conditions is only one of degree. As to the cause of the kidney inflammation, it is probably due to the irritation of toxins, whether those of the disease itself or those which result from the anaphylactic reaction. The latter view would account for the frequent appearance of the condition at a special time, that is in the third or fourth week of the illness. Nephritis has also been attributed to the direct action of the germs themselves, and streptococci have certainly been found present in the kidney. But it seems more rational to attribute the pathological changes in the kidney to the action of the toxins, which may perhaps be excreted in greater quantity at the 'nephritic stage' of the disease. It would be reasonable, however, to assume that any subsequent suppuration is due to the direct action of pyogenic micro-organisms.

The severity of the original attack, curiously enough, plays little or no part in determining the occurrence of nephritis or albuminuria. Both may appear after the most trivial attacks. Often, indeed, the most fatal cases are those which follow an attack of scarlatina which has been altogether overlooked, desquamation perhaps giving the indication of the cause of the trouble. Such patients, no doubt, have been insufficiently looked after and exposed to all sorts of weather variations. This raises the question of the influence of climatic conditions in the production of nephritis. It is beyond all doubt that at certain times of the year both nephritis and albuminuria appear to be much more common, sometimes indeed affecting a comparatively high percentage of patients. Damp cold autumnal weather seems to favour its prevalence, and the largest number of cases in Edinburgh occur in October and November, the percentage incidence being usually highest at that time. The influence of cold in causing scarlatinal nephritis has been denied, but I presume that kidney tissue depressed by the influence of a direct chill in the back would be more susceptible to toxic irritation than is the normal organ. One of my assistants left me to become resident medical officer in a newly-built fever hospital. Of the first twenty scarlatina patients treated no less than sixteen developed nephritis or albuminuria shortly after they were first allowed to sit up in bed. It was found that ventilating outlets, placed above each bed, were acting as inlets, and a most perceptible douche of cold air fell upon the backs of the patients. With the stopping up of these supposed outlets the outbreak of nephritis entirely ceased. In a particular bed of the old hospital buildings in Edinburgh nearly all the children of a susceptible age who occupied it developed nephritis. In this case also a very definite draught concentrated itself on the patient's back when in the sitting

position. Ultimately the bed had to be reserved for adults, and only used when absolutely necessary. While toxins then are, doubtless, the exciting cause of the condition, a predisposing cause may well be exposure to draughts of cold air.

As regards *age*, the second five years of life seems the most susceptible period for kidney trouble, the greatest percentage incidence of undoubted acute nephritis occurring between the ages of five and seven in a recent series of cases. After the age of ten years, while albuminuria is met with fairly frequently, acute nephritis is rare. In any child of under ten years of age who develops nephritis, scarlatina should always be suspected as a probable cause, and desquamation looked for.

As to the *frequency* with which the complication occurs, it is apt to vary in different epidemics. In a series of 4,436 cases, for instance, the percentage incidence of nephritis and late albuminuria taken together was 11.02. In the next 3,172 cases treated the percentage was as low as 5.64, the figures for the complete series of 7,608 patients being 8.78. The second group, however, represented a particularly mild type of the fever, and it is probably unusual for the incidence of kidney complications to be lower than 10 or 11 per cent.

The *period* at which nephritis appears is usually the end of the third week or the beginning of the fourth, say between the sixteenth and the twenty-sixth days. Thus in a series of 134 consecutive cases of acute nephritis, 88 occurred within the ten days named, and of these 68 had their first symptoms between the twentieth and twenty-fourth days inclusive. In rare instances nephritis may appear during the eruptive period. Seldom, however, is it noticed before the tenth day of illness. Albuminuria occurring in the febrile stage of the disease is not included in any of the figures quoted above, being regarded as analogous to the same condition in other diseases. Nephritis is seen more frequently after the twenty-sixth day than it is before the sixteenth, but it is rarely observed after the fortieth. Albuminuria occurring in the later stages of convalescence is perhaps relatively more common.

The *symptoms* of nephritis may now be considered. Very often the first sign of the condition is a vomit. The importance of noting this in a scarlatinal patient and of promptly examining the urine cannot be over-estimated. In other cases a rise of temperature may be the first warning that something is wrong. Or, in very severe cases, a convulsion may be the first obvious sign, even when the urine of a few hours before contains no albumin. Again, in not a small proportion of cases it is the detection of albumin, or of blood, in the routine examination of the urine which first announces the presence of the complication.

In well-marked cases the *temperature* is usually more or less elevated for the first few days. Very irregular in its course, it often shows a tendency to 'spike', being raised at night and normal in the morning. Curiously enough, however, I have seen very few examples of this spiking in the cases of nephritis treated at the City Hospital in the last three years. The chart annexed (Fig. 17) illustrates the irregular pyrexia sometimes noticed. Many patients, on the other hand, have little or no fever, and even when it is present the temperature seldom remains elevated for long. The *pulse*

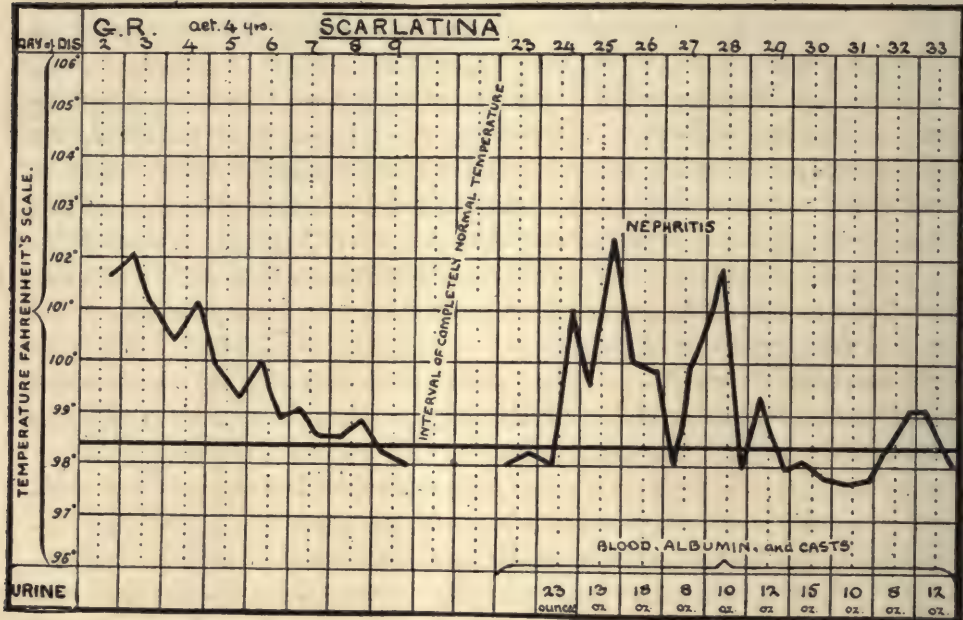


FIG. 17. Nephritis following simple scarlatina. Illustrating the irregular temperature commonly seen in this condition, sometimes elevated, sometimes normal, and with some tendency to 'spiking'.

is usually high in tension, but this feature is not invariable. It is at first accelerated, but as the case progresses it not infrequently becomes extremely slow. The respirations may be increased in frequency in the febrile stage.

In all cases the *urine* is much decreased in amount from the first; when the condition is severe it may be totally suppressed, or only two or three ounces excreted in the twenty-four hours. It usually, but not always, contains blood, the amount of which varies much in quantity, the colour being anything from very slightly 'smoky' to dark reddish brown. Epithelial, hyaline, and blood casts will be found on microscopic examination. The amount of blood and albumin do not appear to have any exact

relation. Often when a large amount of blood is present there seems to be only a comparatively small quantity of albumin. The diminution in the amount of urine continues in most cases for a week at least, and a patient may make a good recovery, even when, during the whole of that period, only a few ounces are passed daily. On one occasion I remember complete suppression lasting for five days followed by recovery. It is needless to say the patient's skin was acting very freely the whole time.

If the case is not treated actively from the first *anasarca* is noticed early. The face, which is from the first pale, becomes swollen and puffy, particularly about the eyelids. Marked œdema of both feet and hands is often seen, and the genitals may be much swollen. But in hospital practice the condition is usually treated too soon for much *anasarca* to develop, and unless a desquamating patient is admitted with well-marked nephritis I find it most difficult to demonstrate the typical appearances of the condition to students. All that I am usually able to show is a child with a pale, pasty, and very slightly puffy face.

Of other symptoms headache is usually present from the first and the patient is often drowsy. When well-marked uræmia establishes itself, convulsions are liable to occur and not infrequently terminate the case. Œdema of the lungs is seen in very severe cases and, in my experience, is invariably fatal. Œdema of the glottis, a possible cause of death, is extremely uncommon in hospital.

The vast majority of cases of nephritis recover completely. The natural action of the kidneys is restored early, and a normal amount of urine is passed after the first ten days or so. Blood and albumin may persist, however, though not usually in very large quantities, for from two to six weeks. In exceptional cases it is longer before the urine is normal, but I have not discharged more than three or four patients with albumin in the urine during the last twenty years, and the maximum detention of a scarlatinal case for this cause certainly does not exceed fourteen weeks. I have seen one instance of chronic nephritis result from scarlatina. The patient in that case was an adult, and died of her illness two years later. I am, however, unable to say in what proportion of cases, if any, albuminuria returns later on. The failings of fever hospitals are so frequently insisted on that I can hardly believe that I would not hear of such sequelæ, if they existed.

Arthritis. The chief joint affection in scarlatina is the so-called 'scarlatinal rheumatism', which is a relatively common complication of the disease. It does not resemble closely true articular rheumatism, and is peculiar in picking out for attack the smaller rather than the larger joints.

It does not appear, moreover, to be influenced by the administration of salicylates, which in many cases quite fail to relieve the pain. It has been aptly compared to the arthritis observed in serum sickness and, like the latter, is probably toxic in origin. The lesion apparently consists of a slight degree of serous effusion into the joints accompanied by some peri-articular swelling and thickening. The theory that it depends on a mild septic infection, not sufficient to cause suppuration, does not appear to be tenable, as McLure, who has investigated this point very carefully, found the fluid was always sterile. It must be remembered that all cases of arthritis observed in the course of scarlet fever are not invariably of this type. Persons who have suffered previously from rheumatic fever are almost sure to develop the complication if they contract the fever, and in their case the condition often appears to have a more close resemblance to true rheumatism. Possibly in such individuals there may be a special vulnerability of the joints, and it need not be assumed that the two conditions have any direct relationship.

Arthritis occurs in roughly 4 per cent. of the total cases ; in a series of 10,000 patients treated in the Edinburgh City Hospital, 3.6 per cent. developed the complication. More than half the patients are over ten years of age, and, considering the age-incidence of scarlatina itself, it is clear that the liability to arthritis is increased after that time of life. Adolescents are very frequently attacked, and females are more apt to suffer than males. The complication usually occurs early in the second week of illness. It may appear, however, as soon as the fourth or fifth day, and before the eruption has disappeared, and it is occasionally met with late in convalescence. In a series of cases the ninth day was found to be the most usual for the appearance of the first symptoms.

The small joints of the fingers and wrists suffer most ; next in frequency probably the small joints of the shoulders and the ankles and knees. Almost any articulation, however, may be affected, and even the joints of the vertebral column are said sometimes to become involved. There is only slight swelling and redness ; indeed, both may be entirely absent, and often the only prominent symptoms are pain and pyrexia. The pain is fairly severe and there is much stiffness and discomfort complained of, even in the milder cases. Several joints are usually affected simultaneously. The temperature is seldom very high, and varies much in character. In mild cases it may assume the somewhat remittent type shown on the chart (Fig. 18). In others it may be more continuous and be maintained at a level of 102 or 103 degrees. There is little or no sweating. The condition is very short lived, often disappearing entirely in three or four days and being

seldom prolonged for more than a week. In rarer instances it may be protracted for a fortnight or even longer (see also Fig. 11, p. 95).

Suppuration in a joint is in my experience most uncommon. I cannot remember seeing more than two or three cases, and they all occurred in the septic form of the disease. But, even after an attack of scarlatina simplex, joints occasionally suppurate, and, in such an event, the cause must be regarded as some secondary infection. Cases which develop chronic 'white swelling' are probably tubercular.

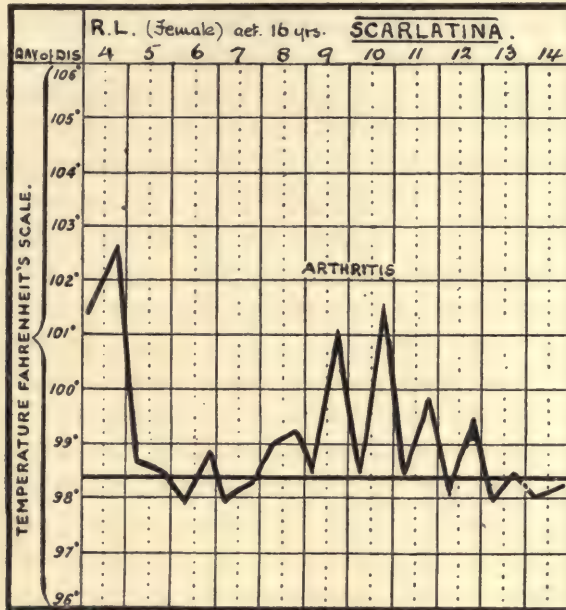


FIG. 18. Showing fever, in convalescence of scarlatina, due to arthritis. Note also unusual critical termination of original fever.

Due to the same cause, doubtless, as the arthritis is the *muscular rheumatism* which in some patients appears to take its place. This has been described as a myositis, probably due to toxins. The muscles affected are most frequently those of the loins, the patient suffering from very severe lumbago. But the abdominal muscles, the muscles of the back and shoulders, and even the intercostals, may participate in the process, and the patient can hardly move or even breathe without discomfort. I have only seen a few instances of this form of rheumatism, which appeared at the typical arthritic period in all the cases, and in which I take a most personal interest, having been a victim myself.

Heart complications. These, when they occur, are more likely to

be met with in patients suffering from arthritis, but occasionally they are observed independently of that complication. They are by no means common in scarlatina; indeed the old teaching which put the fever almost on a par with acute rheumatism as a frequent cause of heart disease is quite unjustified. *Endocarditis* was only noted in 0.58 per cent. of 22,096 cases treated in the Metropolitan Asylums Board Hospitals, and so far as my observation goes is even more rare in Edinburgh. McCollom only observed it thrice in a thousand cases. Soft systolic murmurs, however, are not infrequently present, but are of little or no importance. They may be accompanied by bradycardia and irregularity of the pulse, and are probably due to cardiac myasthenia. True endocarditis is usually febrile and the pulse tends to be rapid. *Pericarditis* is even more uncommon. When it occurs, it is usually in a case of the septic type.

In some cases of otherwise unexplained temperature during the convalescence of scarlatina I have found slight endocarditis to be present. With careful treatment the condition appears to run a favourable course, and I cannot believe that many of the patients whom I have seen affected are likely to suffer from any subsequent cardiac trouble.

Adenitis. Enlargement of the glands is of course often noticed in the acute stage of the illness, while the throat is still inflamed, and, as we have seen, large masses of glands with infiltration and cellulitis of the surrounding structures must be regarded as an ordinary feature in the septic type of the fever. But it is usual to distinguish what may be called 'late adenitis', a condition which may occur at any period during the desquamative stage, and which is often totally independent of any obvious lesion in the fauces. The enlargement of the glands is almost invariably associated with some pyrexia, which at night may attain levels which seem quite disproportionate to the amount of local swelling. Rises of temperature, indeed, in the convalescence of scarlatina will often be found to depend upon a very slight enlargement of a cervical gland. There is usually slight tenderness, and occasionally the inflammation progresses to suppuration. The most common period for this late adenitis is during the third and fourth weeks of the fever, and it may be found in patients suffering from nephritis or albuminuria. Like these renal conditions, it may be due to the irritation of toxins, but Hunter holds that its occurrence is very markedly influenced by oral sepsis, and that attention to the anti-sepsis of the mouth will to some extent obviate it. The pyrexia occasioned by this glandular enlargement is seldom of long duration (Figs. 11, 19). Adenitis occurs in about 13 per cent. of the cases.

Otitis media. This serious complication is extremely common in septic

scarlatina, and is also frequently observed in the stage of convalescence after an ordinary attack. It occurred in 12 per cent. of a series of 4,889 consecutive cases, but in the next series of 10,092 cases the percentage was reduced to 7.3 and was, indeed, as low as 6.8 for the last 7,000 cases in that group. While alteration in the type of the fever may in part be responsible for this improvement, it is probable that the reduction was assisted by the greater precautions taken against the spread of septic infection. It usually appears early, within three weeks of the onset of the fever, but sometimes

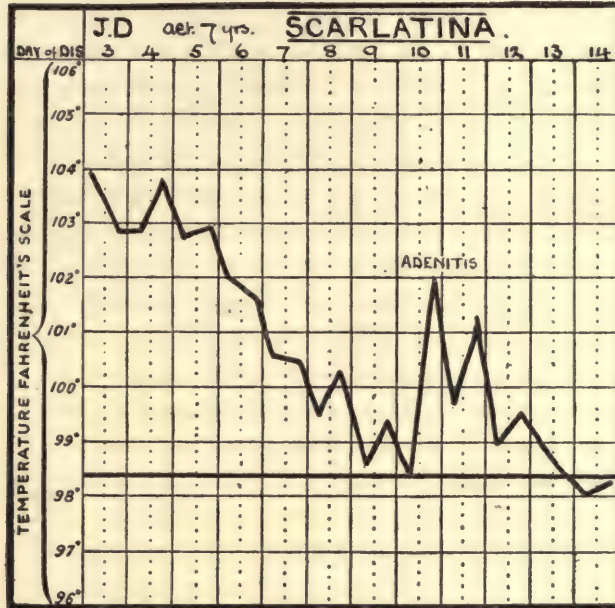


FIG. 19. Showing elevation of temperature due to adenitis following simple scarlatina.

develops in late convalescence. In many cases no doubt the path of infection is through the Eustachian tubes, and it cannot be sufficiently emphasized that forcible syringing of the nasal passages is very liable to assist such a process. In other patients the inflammation may be due to toxæmia, or to septic germs carried by the blood, and it may be remarked here that primary affections of the internal ear, which are very rare in scarlatina, are probably caused by the toxins of the disease. The inflammation, as it affects the middle ear, may be catarrhal or purulent. In the former the exudation is merely serous, and the condition may subside early without serious trouble. More frequently, however, the inflammation is acute and involves the whole middle ear, causing not only inflammation of the mucosa

but actual osteitis. Suppuration occurs and the tympanum is early perforated. The otitis is not uncommonly double.

The symptoms of commencing otitis are fever and pain in the affected ear. But pain is by no means always present, and a moderate pyrexia is sometimes the only prodromal sign. In some cases the discharge itself is the first and only manifestation of the condition, the temperature remaining unaffected. The glands below the ear are often somewhat enlarged. The fever and other symptoms usually subside rapidly with the establishment of the discharge. There is in most cases some temporary deafness.

The otorrhœa itself may be very persistent, sometimes lasting for months. In many cases, on the other hand, the tendency from the first seems to be towards cure, and the discharge may entirely cease in a week or a fortnight. This is particularly the case in older children and adults. It is young children who suffer most from otitis, and who are most likely to develop mastoid trouble. A *superficial mastoid abscess* is a relatively common complication. There is some redness and swelling behind the ear, the auricle is projected outwards till it is almost at right angles to the head, and great tenderness is appreciated when the part is palpated. As a rule, fluctuation is soon evident in such cases, and the pus is found collected beneath the periosteum. In a few cases some exfoliation of bone takes place. Occasionally the pus will be found to be quite superficial. In this case the abscess is due to the suppuration of a gland, and the true mastoid abscess has been merely imitated. An interesting peculiarity of the œdema sometimes observed in this condition is that it is not infrequently first noted in the eyelids of the affected side and over the zygoma, the fascial attachments of which determine its path forwards. Such œdema usually rapidly subsides with division of the periosteum behind the ear, in which situation there may have been little or no swelling.

Acute suppuration of the mastoid cells occasionally results from the otitis. Such symptoms as high temperature, rigors, vomiting, and irritability may call attention to its presence, and there is usually great tenderness at the tip of the mastoid process. Still more serious sequelæ are meningitis, cerebral abscess, of which I have only seen one instance (with complete recovery after operation), thrombosis of the lateral sinus, and permanent damage to the middle ear with total deafness.

Deafness, while often obvious at first, usually passes off quickly, and in my experience, which corroborates that of Goodall, it is extremely rare for a patient to leave hospital deaf. Nor do I believe that much subsequent trouble occurs in the great majority of the patients who have suffered from otorrhœa. As regards the persistence of the discharge, it usually ceases

within ten weeks of the onset of the fever. I am accustomed to detain patients for about fourteen weeks, if necessary, and it is most unusual for me to have to permit a patient to leave hospital with a discharging ear. It is true, no doubt, that the otorrhœa may recur at intervals for some months. Indeed its recurrence in this manner seems to be occasionally responsible for 'return' cases. In very young children deaf mutism occasionally results from the condition.

A word may be added as to the bacteriology of ear discharges. The presence of diphtheroid bacilli in the pus from scarlatinal ears has been noted by many observers, and the bacillus of diphtheria itself may occasionally be present. But most of these organisms may be detected in normal ears, Graham Smith having found them in 66 per cent. of ears examined, his cases including both patients with scarlatinal discharges and normal persons. It must not be assumed then that the presence of a diphtheroid organism, even when showing definite polar staining, means necessarily that the patient is a 'carrier' of that disease. Careful cultural tests, and animal experiments checked by control tests with antitoxin, are necessary for the differentiation.

The other groups of organisms usually found in these discharges are streptococci, pneumococci, and staphylococci. It is rare to find only one variety of bacteria present.

Rhinitis. Purulent discharge from the nose is often a troublesome complication in the convalescence of scarlatina. It occurs most frequently in the youngest patients, and is especially frequent in those who suffer from adenoids, and in those who are pulled down as the result of the fever. It is undoubtedly infective from patient to patient and is very troublesome in hospital practice. It is extremely persistent, resisting treatment, and plays a prominent part in the production of the 'return' case. The discharge is often of a highly irritating nature, excoriating the orifices of the nostrils, and making them raw and scabby. It occurs in about 8 per cent. of my cases, including those of the septic type, in which, of course, it is present from the first. The bacteriology of the discharge is much the same as that of the ear, but true diphtheria bacilli occur more frequently and, although no general infection results, the effects of antitoxin on the discharge suggests that they may play some part in causing the condition.

Vaginitis is also occasionally seen in weakly children, and, like rhinitis, unless care is taken, it is infective from patient to patient. It was not infrequently seen in our old buildings, but since we have occupied the new hospital with its ample floor space it is now almost unknown. When it occurs it is probably often the result of auto-inoculation with septic material

from the nose or ear. It may be sometimes troublesome and persistent, and during its continuance the isolation of the patient should be maintained.

Other complications. We have seen that *broncho-pneumonia* may play some part in causing death in septic cases. More rarely it may appear during the desquamative period of an ordinary case. It is occasionally severe, but, in my experience, is usually trivial when compared with the same complication supervening in measles or whooping-cough. A more frequent complication of convalescence is *septic tonsillitis*, which is most liable to occur in young children, and may be followed by glandular enlargements, rhinitis, and all the symptoms of a primary septic attack. The tonsils may be inflamed, patched, or actually ulcerated. In hospital the question of infection from neighbouring septic cases must not be lost sight of, as in some instances, at least, there can be little doubt that the tonsillitis is due to such a cause. *Ulcerative stomatitis* may occur either in the course of a septic case or quite independently in convalescence. The gums are swollen and spongy and often bleed freely. Aphthous-looking patches appear on the lips, buccal mucous membrane, and tongue, and often develop into small ulcers. The teeth may be loosened and even fall out. The mouth is extremely painful when the patient attempts to take food. *Cancrum oris* is fortunately rare. I have only seen two instances of it in over 20,000 cases of scarlatina. In both it occurred in markedly septic cases and followed an ulcerative stomatitis of the kind just described. A slight degree of *jaundice* is not very uncommon in the course of the illness, and Goldie has recently noted its coexistence with some degree of pancreatitis. A tendency to a yellowish colour of the skin is a well-marked feature in many patients at the time of, and just after, the eruption. I have seen only a few cases of *purpura hæmorrhagica*, always in septic cases and usually supervening in the third week. In one of these, except for traces of blood in the urine for three or four days previously, the illness appeared suddenly with hæmatemesis and subcutaneous hæmorrhages of considerable size, and ran to a fatal termination within three days. Rolleston, McCririck and others have described cases of the rapidly fatal type of the disease known as 'purpura fulminans' in which the ecchymoses are large and inflammatory and no bleeding from the mucous membranes occurs. *Chorea* and various nervous sequelæ have been described as following scarlatina, as is the case with the other fevers. In my experience they have been rare, and it is possible their occurrence was a mere coincidence. Recently I have seen in a young female adult right sided *hemiplegia* with aphasia. We attributed this to toxic encephalitis, although embolism and thrombosis appear to have been responsible for the majority of the 66 cases collected

by Rolleston from the literature. It is, of course, obvious that *meningitis* may occur in patients in whom the middle ear is seriously affected, and I have seen one fatal streptococcal case in which the ears were reported to be normal by an otologist.

Post-Scarlatinal Diphtheria. The convalescence of scarlet fever may be interrupted by an attack of almost any infectious disease. Its association, however, with diphtheria presents many points of special interest. A patient suffering from either of these infections appears particularly liable to contract the other. Very often the two diseases are associated from the first, either separately in different members of the same family or together in any one person. For instance, in the year 1907, out of 1,039 cases of scarlatina treated in the City Hospital, twenty were found to be suffering from concurrent diphtheria on admission.

More troublesome, however, to hospital authorities are the cases of diphtheria that appear during the stage of convalescence. Fortunately, the introduction of serum-treatment has almost abolished the terrible mortality which used to be so characteristic of this dangerous sequela. Post-scarlatinal diphtheria may be for practical purposes regarded as a hospital phenomenon, that is to say, it occurs much more rarely in private practice. Introduction by carriers is the obvious explanation, and it may be mentioned that in different years from 10 to 15 per cent. of Edinburgh scarlet-fever patients are proved on admission to harbour the bacillus in the throat. Again, it is perfectly possible that the patient himself may have harboured the bacillus for a long time, and that it has only become active in the convalescent stage of his attack of scarlatina. I should think it very probable that the cases in which the acute stages of the two diseases run concurrently are due to a 'carrier' of the bacillus contracting scarlatina. And, as the greatest susceptibility of a scarlatina patient to diphtheria appears to be in his fourth week, it is quite conceivable that the post-scarlatinal infection is sometimes due to this cause. Outbreaks of this complication appear to be influenced by climatic conditions, the cases cropping up in different wards of the same hospital in damp cold weather, as has been pointed out by Foord Caiger. Overcrowding is also liable to influence their occurrence, as might only be expected in wards in which one or more of the patients may harbour the bacillus. As mentioned above, the complication, if untreated with serum, runs a severe course and is particularly liable to affect the larynx. Recognized early and treated promptly it is, of course, much less serious, but there is no doubt that, even under such favourable circumstances, it should never be regarded lightly.

DIAGNOSIS. Scarlatina is so varied in its manifestations, and is

liable on occasion to assume such mild forms, that the diagnosis is often extremely difficult. We may for purposes of convenience consider its possibilities first during the invasion stage, secondly during the eruptive period, and last after the more obvious symptoms have subsided. As regards the symptoms of *invasion*, we have already noted that the more or less simultaneous occurrence of sore throat, headache, and vomiting should cause the medical attendant to be suspicious, and when these three symptoms are present it is his duty to eliminate scarlatina before thinking of anything else. The early rise of the temperature to comparatively high levels, as shown in the charts (Figs. 9, 10, 11), and still more a pulse more rapid than such pyrexia would warrant, will make the case still more suggestive. Even at this early stage the scarlatinal facies may be well marked, and circumoral pallor a prominent feature. The tongue is, moreover, heavily coated, and the fungiform papillæ may be already oedematous. Any suggestion of punctation on the soft palate will make such a case fairly clear, but no definite diagnosis can be made till the rash appears. As this is seldom delayed for more than twenty-four hours the practitioner will do well to pay a second visit shortly after his first, having previously given directions that, by the use of hot baths, or blankets with hot bottles, everything possible be done to induce the expected eruption to make its appearance. At this stage of the illness, even if the throat is not patched, it is well to think of a commencing diphtheria, the other most frequently mistaken conditions being acute tonsillitis and lobar pneumonia in children, any of which may have a similar onset, although in tonsillitis it is not usual for the symptoms to be so acute. Without acute symptoms it is unlikely that scarlatina itself will be suspected at this early period.

When the *eruption* has appeared diagnosis is in most cases fairly easy, particularly so if most of the characteristic initial symptoms have been present, and the condition of the throat and tongue is at all suggestive. It is well to remember that the almost complete absence of fever need not necessarily affect the diagnosis (see Fig. 12), provided the other symptoms are fairly typical. If, when other signs are in favour of scarlatina, the absence of a rash on the trunk makes the practitioner hesitate, he must remember that he has not examined a patient properly until he has examined the whole body. A definite rash, for instance, may be still visible on the legs. As regards the distinction of the rash itself from those caused by other conditions, the reader is referred to the following section on differential diagnosis. As to the tongue, it is well to recollect that the 'white strawberry' tongue may be imitated in many conditions, notably in diphtheria and measles. But in those infections the progressive desquamation of the

fur, till a 'red strawberry' type is reached, is not seen. The real diagnostic tongue is the 'red strawberry', or, as I am inclined to describe it, 'the fourth day and after' tongue. A typical tongue of this type needs very few other corroborative details to make a certain diagnosis, but it must be admitted that, in some cases, it does not, so to speak, reach its full development. Nevertheless, prominent fungiform papillæ are of great value in diagnosis, and McCollom found them to be the only constant symptom in over a thousand cases of scarlatina.

At any period of a case of scarlatina the medical attendant must be prepared to find that one or more, perhaps indeed many, of what he has been accustomed to regard as cardinal symptoms may be wanting. Thus he may never see a definite rash, or there may be no fever, or visible desquamation may be entirely absent. Again, a patient may not complain of his throat, and such symptoms as headache and vomiting may have never occurred. In the vast majority of cases, however, enough signs will be present to make a diagnosis.

After the acute stage is over the diagnosis has often yet to be made. It is not unusual for a medical man to be consulted for the first time after the eruptive period is over. If the symptoms are fairly recent, information may be obtained from the condition of the tongue, which perhaps will be still clean and red, even though the papillæ may no longer be prominent. Traces of the rash may be seen as stained lines in the flexures of the larger joints; or the somewhat pink papulation of the skin of the arms and legs, particularly the latter, may yet be visible. Such signs taken in conjunction with a suggestive history, and especially with known infection in the house, would at once clear up the case. I differ, I think, from many of my colleagues in this country in believing that there is something to be said in favour of the so-called *Rumpel-Leede sign*. These observers found that if a bandage, and for this purpose an ordinary Domette bandage does very well, is applied to the upper arm, sufficiently tightly to obstruct the venous return without obliterating completely the radial pulse, and is left in position for from five to fifteen minutes, numerous minute petechial hæmorrhages appear in the fold of the elbow. Richardson, using this test at the Edinburgh City Hospital in several hundred cases, came to the conclusion that the petechiæ can be produced in every scarlet fever case in the first fortnight of illness, that they occur also after other rashes but only for three or four days, and that a negative result practically excludes scarlet fever. I can, within limits, confirm these results, and, while by no means reposing entire confidence in the test, have used it to supplement the more usual methods of diagnosis.

Later, we may have to diagnose by desquamation alone. This is extremely hazardous, indeed impossible, if there is not some history of illness to help us. But if we can date from an attack of sore throat, or of vomiting, or of a so-called erythema, and find that the situation and character of the desquamation correspond with that which would fairly be expected in scarlatina after a similar interval (see p. 103), then I think a definite opinion is certainly justified.

The occurrence of such suggestive symptoms as arthritis, nephritis, albuminuria or otorrhœa, in a case presenting doubtful desquamation, would obviously be of great assistance.

Differential diagnosis. During the pre-eruptive period we have to distinguish scarlatina from simple *tonsillitis*. This from the throat appearances alone is almost, if not quite, impossible. The constitutional symptoms in the less serious condition are seldom so severe, and such a sign as vomiting would be much in favour of scarlatina. Any marked unilateral swelling would usually distinguish a quinsy, in which constitutional disturbance is often considerable. Acute *lobar pneumonia* is frequently sent in to the City Hospital as scarlatina. The patients are always young children, who almost invariably have a scarlatinal facies, and who have commenced their illness with headache, vomiting, shivering, and high fever. The rapidity of the pulse in proportion to the temperature may be well marked in such patients. In most cases a pink flush on the skin taken in conjunction with the other points mentioned has, doubtless, caused the error. If there is any rapidity of respiration the lung condition should be suspected and it is well not to notify till a really definite rash is present. The examination of the chest may be practically negative for some days. Ultimately, of course, it gives positive information as to the cause of the fever. The possibility of the throat and fever being due to *influenza* must also be considered. The pulse, however, is often slow in that disease, and well-marked frontal headache and pain in the back might suggest it. Again, the soft palate, as a rule, shows less injection in influenza. Definite erythematous rashes, sometimes very suggestive of scarlet fever, are seen in not a few cases, but their distribution is irregular and they are usually limited to the trunk. I have, however, seen one on the limbs of a patient whose trunk was completely spared.

In the acute stage of the fever we may, especially if the rash has disappeared, have to distinguish scarlatina from *diphtheria*. The differential diagnosis will be found fully discussed under the latter disease (p. 416). It will be sufficient to say here that the rashes seen in diphtheria are not, as a rule, so punctiform or so general in their distribution as that of scar-

latina, that in the latter disease the patches on the throat wipe off readily and are apt to leave superficial ulcerations behind them, and that, while the 'white strawberry' tongue is often seen in diphtheria, it does not peel characteristically. Help may also be obtained from bacteriological examination, but the fact that the two diseases may run their course concurrently must never be lost sight of.

Except for diphtheria the differential diagnosis of scarlatina in the acute stage depends upon the distinction of the eruption from others which may resemble it. First, then, it will be well to consider the other *exanthemata*.

Measles is under certain circumstances liable to be mistaken for scarlatina, firstly, because it may occasionally present a prodromal rash of a scarlatinal type, secondly, from the confluence of its true eruption. Scarlatina, on the other hand, is not infrequently regarded as measles, chiefly on account of the blotchy character its rash may assume upon the extremities, especially in the septic variety of the fever (see Pl. IX). As regards the prodromal rash, it is more diffuse, and less punctate, than that of scarlatina, and the catarrhal symptoms of the patient and the probable presence of Koplik's spots, stomatitis, or gingivitis in the mouth should make the diagnosis reasonably easy. At the height of the disease, also, the inflamed state of the mouth will point to measles. As to the eruption, the distinctions are discussed elsewhere (p. 54), and it need only be said that definite spotting or staining in the circumoral region practically excludes scarlatina, and, even when the measles rash has become confluent on the trunk, this sign is seldom absent. The condition of the tongue, the rate of the respirations, nearly always rapid in a measles with a confluent eruption, and the suffused eyes and bleared expression will still further distinguish the two fevers.

Much more difficult is the diagnosis from *rubella*. This is fully considered elsewhere (p. 78). It is the cases of rubella which come under observation on the second day of their eruption which are mistaken for scarlatina. On the first day the rash is too definitely spotted on the face to cause difficulty. Unfortunately, however, it does not leave staining behind it, and a few hours later the circumoral region may be quite clear. The polymorphous character of the rubella rash, the absence of really fine punctation, and the rarity of marked constitutional symptoms, taken in conjunction with the practically normal tongue and slightly suffused conjunctiva, the latter not to be seen in mild scarlatina, will all be of assistance. The presence of stiff-neck, with little or no throat symptoms, and the general enlargement of glands are also worth consideration.

The prodromal rashes of *small-pox* may cause difficulty (see p. 160).

Of the two rashes liable to be confused with scarlatina the simple scarlatiniform flush should not give much trouble. It is only seldom punctate, and that very faintly, and is more irregularly distributed. The main symptoms which carry weight are the throat and tongue, neither of which in the prodromal fever of small-pox is likely to resemble those of scarlatina. Definite pain in the back suggests the more grave disease. The more serious, almost erysipelatous, lobster rash occasionally resembles closely a severe case of scarlatina, though here again the distribution is apt to be irregular and the face of the patient is more puffy and uniformly congested. Hæmorrhages and petechial spots are also liable to be associated with it. For other points the section on small-pox may be consulted.

The scarlatiniform prodromal rash of *chicken-pox* is a frequent cause of the latter disease being notified as scarlatina. Not a year passes without two or three such cases being admitted to the City Hospital. Usually the typical varicella spots appear early, and the question is often whether both diseases are present. In such cases we must be guided by the condition of the throat and tongue, always remembering that, if no other definite signs of scarlatina are present besides the rash, the chances are greatly in favour of the latter being due to the chicken-pox (see pp. 215, 219).

Various forms of *erythema* are frequently mistaken for scarlatina. Of these we have to distinguish the rashes due to drugs, serum rashes, enema rashes, and rashes caused by various articles of food.

Of the *drug rashes* that due to copaiba is perhaps most frequently confused with the scarlatinal eruption which in certain circumstances it very closely resembles, though in others it may present a greater likeness to measles. When scarlatiniform it is sometimes punctate, but, as a rule, the punctuation is not very definite. It is usually distributed universally, but may present irregularities such as urticarial blotches. It may be suspected in young men, who, except for its presence, do not show definite scarlatinal symptoms, and who, not infrequently, will be found to have already suffered from scarlatina, a point which, though perhaps of not much importance, should always suggest that great care be taken before notification. And here it may not be amiss to say that because a copaiba rash is suspected, and because urethral discharge is present, it by no means follows that the patient is not suffering from scarlatina, nor, on the other hand, is it certain, even if scarlatina can be safely dismissed, that copaiba has caused the rash. It seems to be beyond question that rashes, no doubt of a septic nature, and sometimes scarlatiniform, may originate from gonorrhœa alone. I have seen several such, the patients freely acknowledging that they suffered from urethral discharge, but showing prescriptions

PLATE IX.



A scarlet fever rash showing blotching and papulation on the forearm, and presenting a somewhat measly appearance. The colour, however, is more that of scarlet fever.

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which contained no resins at all. In a few cases in my recollection, gonorrhœa was present together with true scarlatina. To return, however, to the question of drugs, scarlatiniform rashes are sometimes due to the use of patent pills, such as Doan's and de Witt's, which contain cubebs or some similar resin. *Quinine* will cause in some persons an eruption which to some extent simulates scarlatina. As a rule, however, the rash is more diffuse, and less punctate. It is liable to be restricted to the trunk, and perhaps the face, which in any case is flushed. The throat sometimes suffers, and headache and dizziness may be present. Sometimes even there is moderate pyrexia, but it must be remembered that the drug has been probably administered with a definite purpose, and that the condition which called for its employment may be still active. In the cases which I have observed, there has been only faint powdering, hardly definite desquamation. *Salicylate of soda* may cause merely a uniform flush, owing to its strong action on the skin, or a fine papulation, as if a miliary sweat rash was commencing. As the diseases in which it is most freely used are often associated with fever and sore throat, the resemblance to scarlatina may be somewhat striking. I have seen the flush on the skin persist for as long as ten days. The desquamation was slight and not of the pinhole type. *Belladonna* causes a uniform brilliant red flush, chiefly seen on the trunk. The face is flushed and the pupils are more or less dilated. I have seen this eruption, not infrequently, when pushing the drug in cases of whooping-cough. At first sight the resemblance to scarlatina is well marked, and, as the pulse is often rapid, and the temperature moderately raised, a mistake might easily be made by one who did not know the circumstances of the case. Of other drugs we may mention morphia and opium, which cause a somewhat scarlatiniform rash, most often on the extremities, though sometimes generally distributed, and accompanied by itching, chloral hydrate, and chrysarobin, which, locally applied, sometimes starts a superficial dermatitis which spreads as a bright red flush a certain distance from the point of application.

In distinguishing these various drug rashes from scarlatina we are influenced firstly by the frequent absence of constitutional symptoms, secondly by the history of the case and the fact that the patient has been treated by particular remedies, and lastly by the want of definite scarlatinal manifestations, such for instance as the tongue, or later the characteristic desquamation. If a resinous substance is suspected of being responsible for the rash, its presence may be detected in the urine, either by the odour, or by precipitation by nitric acid. Irregularities of distribution, or a tendency to a multiform character in the rash itself, would also tell against

a diagnosis of scarlatina. Occasionally the symptoms presented by the patient on examination suggest that he is likely to have been treated with a particular drug. A supposed case of scarlatina, for instance, in whose history rheumatic pains bulk largely, suggests that salicylates may have been given. The presence of a gonorrhœa, if detected, can hardly fail to summon the idea of copaiba or cubebs to the mind of the hospital medical officer, and the general practitioner should, if a rash unexpectedly presents itself in the case which he is attending, recollect that it may possibly be due to some remedy which he has prescribed.

Rashes, the result of the employment of serum, when scarlatiniform in character, perhaps give more trouble than any other differential diagnosis. After some serums these scarlatinal rashes are very common, though, taken all over, they are probably less frequent than the other varieties of erythema which follow the administration of antitoxin. The differential diagnosis of these *serum rashes* will be found fully discussed elsewhere (p. 440). All that need be said here is that a complete absence of constitutional symptoms is against a true scarlatinal infection, and that a rash, spreading from, and most intense near, the site of inoculation, strongly suggests a serum phenomenon. The presence, moreover, of any urticarial patch is practically enough to eliminate scarlatina. The practitioner will do well to be cautious in coming to a diagnosis of scarlatina in a case which has recently received serum treatment.

It is not likely that *enema* rashes, once the possibility of their occurrence is fully recognized, will be a source of much difficulty. They are seldom definitely punctate, and have the irregularity of character and distribution which usually characterize adventitious rashes. Some have a peculiar colour, a slight bluish tone being fairly obvious. In no case are they accompanied by constitutional symptoms, though it must be remembered that the condition for which the enema was required may have been a febrile one. The cause of these rashes has been alleged to be the use of hard, instead of soft, soap in the enema. This is certainly not the case, as I frequently observe them after an irrigation of the large intestine in enteric fever, when only hot water is employed. They appear to me to depend upon the absorption of septic material from the gut. The enema may act both by making the bowel contents more soluble, and by increasing the absorptive powers of the intestinal wall by the clearing away of adherent mucus. That something of this sort occurs is suggested also by the fact that similar rashes occasionally appear after the administration of a saline purge. I have seen them on several occasions after a large dose of Henry's solution.

Various forms of *erythema* may follow the ingestion of certain food substances, some individuals being especially susceptible to particular articles of diet. Shellfish, strawberries, tomatoes, and other foods cause rashes which are only rarely scarlatinal, being, for the most part, definitely urticarial or, at least, presenting urticarial patches in some parts of the body. Except that vomiting may occur with such a rash, constitutional symptoms are usually absent, and it is most unusual to find the temperature raised. The patient himself may often throw light upon the condition, as he, not infrequently, has suffered from similar rashes before.

Lastly, in the *desquamative stage*, the question may arise as to whether the shedding of the cuticle is due to scarlatina or not. This is often a most difficult point. Even 'pinhole' desquamation is occasionally seen in other conditions. The palms and soles of persons who have a tough skin will always tend to desquamate when, for any reason, they are confined to bed, and desquamation, especially of the soles, is observed in many prolonged fevers. I lay most stress myself on the correspondence of the history given by the patient with the stage of his desquamation. Patients sometimes desquamate profusely after simple erythema, measles, rubella, and serum rashes. The history is of great importance in such cases. Skinning between the fingers and splitting of the skin round the nails are highly suggestive of scarlatina. The presence of a suggestively scarlatinal complication is, of course, of great assistance.

PROGNOSIS. The mortality of scarlatina varies largely with the type of epidemic. In this country from 2 to 5 per cent. of the patients succumb. The lowest mortality for any one year in the Edinburgh City Hospital has been 1·2 per cent., the highest just 5 per cent. *Age* exercises a considerable influence. The younger the patient the less, broadly speaking, are the chances of recovery. Caiger, in his table, which refers to 167,840 cases treated in the Metropolitan Asylums Board Hospitals, shows that the mortality of infants of under one year is as high as 21 per cent., and for the next year of life 16 per cent. Thereafter the mortality rapidly declines, reaching 5·5 per cent. for the fifth year, and falling still further to 2·5 per cent. for the second quinquennium. The least fatal age is from ten to fifteen, and from that time there is a slight increase in the mortality, which, however, does not again exceed 2 per cent. till the age of thirty-five is passed. From that time onward a gradual increase in fatality is noted. The death-rate for the whole group of cases is 4·3 per cent., and males appear to have a slightly higher death-rate than females.

Prognosis obviously depends upon the type assumed by the fever in a particular patient. Malignant or 'toxic' cases are practically always

fatal. A poorly-developed, dusky eruption not disappearing well on pressure, a very rapid soft pulse, and hyperpyretic levels of temperature, are extremely grave signs. Regarding cases which stand, as it were, on the border-line of malignity, I have a dread of a white face seen in conjunction with a very intense eruption. In such patients the case may not uncommonly assume an adynamic type a day or two later. A comparatively poor temperature reaction, with a very intense rash and a soft pulse, also makes me anxious. If the pulse remains unduly rapid in proportion to the temperature into the third day of illness there is always cause for some disquietude. The possibility of an apparently simple case suddenly developing toxic symptoms must not be lost sight of.

Much patching of the throat, and intense oedema, must be regarded as bad signs. Too often they presage a septic type of the disease with much glandular enlargement, extensive ulceration, many complications, and a severe course. Discharge from the nose in the early days of the illness nearly always points to the case being thoroughly septic later on. Once there is no doubt that we are dealing with the septic or anginose type, if we succeed in saving three out of four patients we must regard ourselves as very fortunate. In this variety of the illness the prognosis is grave in proportion to the enlargement and hardness of the cervical glands, the persistence and extension of the ulceration of the fauces and palate, and the level maintained by the temperature. Profuse nasal discharge and early implication of the middle ear are also seen in the worst cases. Bronchopneumonia adds much to the risk, and very marked restlessness, insomnia, and the refusal of food are all bad signs. Towards the end the patient, who has usually been flushed, becomes yellowish or pale in the complexion, and the pulse is apt to become extremely rapid.

As regards simple cases, the main risk to be considered is the possibility of the subsequent complications. During the actual fever high temperature levels and a rapid pulse need not cause undue alarm, always provided the colour remains good and the rash is well developed. Patients, indeed, who show a good rash and a good temperature reaction, say 104° to 105° , usually do extremely well. In convalescence, however, *complications* occur frequently enough to be responsible for death in not a few cases, and the prognosis, therefore, must always be guarded to that extent. We are unable to predict in the early days of the illness that any given individual will not ultimately succumb to nephritis or to the complications which may follow otitis media. And such conditions as endocarditis, and still more pericarditis, although fortunately rare, are serious enough when they do occur to make us cautious in assuming that the recovery of any patient is a certainty.

Nephritis, when treated from the first, is perhaps not very fatal. Should, however, its existence remain unsuspected for several days, the patient may be in a most dangerous condition before treatment is undertaken. Most of the deaths which I have witnessed have been in patients whose nephritis first drew the attention of their medical attendant to the fact that they had passed through an unrecognized attack of scarlatina. When there is very marked œdema the outlook is always serious. Still, as has been indicated above, œdema is but seldom seen in patients treated promptly from the first. Initial convulsions, or persistent vomiting, are grave signs, as are convulsions appearing later and œdema of the lungs, the last of which is, indeed, in my experience, invariably fatal. The gravity of the case is, of course, more or less proportionate to the diminution in the amount of the urine. Nevertheless, once the skin and bowels are acting well, too much anxiety need not be caused if only 5 or 6 ounces are passed in the twenty-four hours. Many patients pass even a smaller quantity for many days in succession and yet make good recoveries, and I have already alluded to a patient who survived complete suppression for no less than five days.

The amount of albumin does not influence the prognosis as much as might be expected, nor does the presence or absence of hæmaturia. I have seen patients die who at no time had much more than a trace of albumin, though all the other symptoms of nephritis were present. And, on the other hand, patients will recover, even if their urine practically solidifies on boiling. Some of the worst cases show no blood in the urine, and I am inclined to believe that those with hæmaturia, on the whole, do better than those who, with other nephritic manifestations, fail to present this particular symptom.

Even a trace of albumin in the urine must be taken seriously, especially if it is accompanied with vomiting or any suggestion of puffiness of the face. I have seen two cases, treated from the moment of their first symptom, die within thirty-six hours in uræmic convulsions. Such occurrences are fortunately rare, but their possibility must never be forgotten. Nevertheless, the outlook as regards nephritis is, as a rule, extremely good, and the chances of the albuminuria becoming chronic, especially in children, are exceedingly remote.

The outlook in arthritis is good. Seldom do the joints suppurate, and, even if endocarditis follows, the chances are that, with complete rest and careful treatment, the patient will make a satisfactory recovery. Pericarditis, however, is usually fatal. As regards otitis media, as long as the ear continues to discharge, there is always the chance of mastoid

trouble and even worse complications. Deafness, however, seldom follows an uncomplicated case. As regards the risks of remote effects of the fever, recent work by Dublin goes to show that for three years after scarlet fever the death-rate is no higher than that normally expected.

TREATMENT. Under this head fall to be considered the general management of the case, the main principles of treatment, the selection of a suitable diet, the local applications to the throat, and, lastly, the methods of dealing with the various complications.

Management. The *isolation* of the patient is the first essential. This can be quite satisfactorily carried out in houses where it is possible to set aside the whole upper flat for the patient and nurse. It is hardly so safe when the door opens on a landing frequented by other members of the family. A carbolized sheet hung over the doorway may be useful in emphasizing the presence of an infectious case, and the precaution is so hallowed by custom that the young practitioner might be criticized for dispensing with it. Its practical value is more than doubtful, and it may be added any draught of air tends to flow *into* the room if, as always should be the case, a fire is burning there. All utensils should be disinfected, relatives should be rigidly excluded, and the medical attendant must wear an overall cloak on his visits. The room, if possible, should be large and well ventilated.

The majority of patients are nowadays treated in hospital. Aggregation has its disadvantages, and an adequate amount of floor space, say 144 square feet as a minimum, is requisite, if it is to be carried out safely. Septic cases should, so far as possible, be isolated, or surrounded with special precautions. Convalescent wards should be reserved for 'clean' cases. The reader is referred to page 603 for a fuller discussion of the difficulties of hospital management.

It is my custom to keep the patient in *bed for three weeks* from admission. As he comes into hospital, on an average, on his third day, this implies that he is not allowed to rise till he is past the most likely nephritic period. By this rule he is less exposed to changes of temperature, and the precaution is at least a reasonable one. On the other hand, it is well in private practice, if children are inclined to jump out of bed as soon as the nurse's back is turned, to allow them up properly clothed rather than to risk their exposure when insufficiently protected. A little more latitude may be allowed to adults, who may reasonably be expected to exercise their common sense if they are permitted to be out of bed after a fortnight. The patient should in all cases wear a flannel bedgown, and during the winter months it may be advisable to allow delicate children who are inclined

to sit up in bed a light suit of combinations in addition. If the weather is dry there is no reason to keep patients indoors when they have been out of bed for a week. In damp weather it is wise to be careful how this privilege is extended to children, especially those at the 'nephritic' age. In children it is a good plan to cut the hair short as a routine. In adult women it is doubtful whether this should be done. Much hair is usually lost in any case.

To assist elimination in every possible way attention should be paid to the condition of the skin throughout the whole illness. Soap and water washing in bed daily from the first, and frequent sponges while the temperature is raised, are essential. Later, baths may be given at intervals and the spongings restricted to morning and evening. This serves to keep the skin in good order, and it is likely to perform its functions better in consequence. The removal of the separated cuticle also frees the pores. Recently there has been much discussion of the *inunction* treatment advocated by Milne. This consists of gently rubbing in pure eucalyptus oil, all over the body from the crown of the head to the soles of the feet, twice daily for the first four days of illness, and thereafter once daily until the tenth day. For the first twenty-four hours a 1-10 carbolic oil swabbing of the throat is practised two-hourly. Milne claims that patients so treated may be allowed from the first to mix freely with susceptible persons with no fear of infection, and that all complications are prevented. It is only natural that a system, so cheap in comparison with that of hospital isolation, should have obtained a certain measure of support. But the fever hospitals which have tried the method have found that, even when applied from the first in ward outbreaks of the disease, it cannot be relied upon to prevent infection, and that, when used systematically in the treatment of large numbers of patients, it prevents neither the development of complications nor the occurrence of return cases. It must be remembered that scarlatina is not a very highly infectious disease, and the value of the treatment seems to me to have been exaggerated from a want of appreciation of this fact. Again, carbolic oil is not a very powerful antiseptic, and the necessity for skin inunction does not appear to be great now that the probability of infection by means of desquamated scales is being generally discredited.

General Treatment. During the febrile stage the comfort of the patient is the main consideration. If any drugs are used, a mixture of acetate of ammonia with either sal volatile or nitrous ether may be given, as it helps to improve the action of the skin. The tepid sponge should be frequently used if the temperature is high. I am old-fashioned enough to like to see the rash well developed, and should it be scanty or of a bad

colour I am accustomed to apply fomentations of mustard and hot water over the trunk, or pack the patient in blankets and hot bottles. I am quite convinced of the inestimable value of small doses of alcohol, in the form of whisky or brandy, which I often prescribe with the object of dilating the skin capillaries and promoting the development of the eruption. For the same reason, should hyperpyrexia develop in a case in which the rash is scanty or dusky, I prefer hot applications to the body surface, rather than cold, and apply ice to the head only. If the skin can only be induced to act freely, the temperature will often relax. Except in toxic and septic cases, which will be considered later, the pulse is not likely to require much attention. Sleeplessness and restlessness may call for treatment. In adults bromidia or veronal often give good results. For children I usually try first a little hot toddy, which frequently has the desired effect, and acts well on the skin in addition. Frequent sponging with warm water will also assist sleep. Paraldehyde, given by the rectum, is most useful, especially in young subjects.

There are no drugs capable of modifying the course of scarlatina. Various general antiseptics, notably sulpho-carbolate of soda, have been tried, but none of these have, in my hands, given good results.

Dietetic Treatment. In our treatment of any of the acute fevers it is necessary to keep in view the conditions which may complicate its course and convalescence. Were it not for this there would be but little to say respecting the diet of scarlatina, and, even as it is, many hold the view that this fever may be dieted on the same lines as any other acute infection. For many years, however, physicians, in prescribing a diet for scarlatina patients, have been influenced by the comparative frequency with which acute nephritis and albuminuria are liable to occur in its convalescent stage, and many of the dietaries suggested have been, therefore, devised to act as a prophylactic measure against this particular complication.

In the *acute stage* the fever is so brief that the patient may be expected to maintain his strength quite satisfactorily on a fluid régime. During the first twenty-four hours vomiting is so frequent that he may well be left alone. Later, after the appearance of the rash, milk is, as a rule, quite sufficient. It should be given with the same precautions as are indicated in the subsequent chapter on enteric fever. I am not accustomed to give meat broths at this stage. If allowed at all, they should be made weak. Water should be supplied freely to the patient, and there is no objection to the use of alkaline aerated waters, should he prefer them. Fruit juices to flavour the drinks are often very refreshing, and their use

may be encouraged. Weak tea may also be allowed in moderation and is much appreciated by female adults.

In the more prolonged forms of the fever, in septic scarlatina for example, it may be advisable to allow somewhat more than a purely milk diet. Arrowroot and other starchy foods, thin oatmeal gruel, Benger's food, and other similar preparations may all be given, as may well-stewed fruit, if it can be swallowed. The difficulty, indeed, often is, in the septic form of the fever, for a patient with an acutely inflamed throat to swallow anything but fluids. Occasionally fluids themselves cannot be taken in sufficient quantity to adequately nourish the patient. In such cases nasal feeding must be resorted to, and its systematic use has often a very beneficial effect on the condition of the mouth and fauces, which, being thoroughly rested, and also relieved from the fermentative action of food substances clinging to them, sometimes clean up with remarkable rapidity. Broadly speaking, I consider the use of meat extracts and beaten-up eggs undesirable in the acute stage of scarlatina, but there is no need to hesitate to prescribe either should the patient appear to be inadequately supported on the above diet. Alcohol, again, is usually to be avoided, but in the septic type of the fever it is, not infrequently, necessary.

The toxic type of scarlatina offers few opportunities for dietetic treatment. Vomiting is often so persistent that we may be reduced to rectal feeding. As, however, diarrhoea is also present in many cases, even this may be found to be impossible. Everything should be done to force fluids on the patient, if his stomach allows it, and, if not, they may occasionally be given by the bowel. Stimulation, preferably with brandy or, perhaps, champagne, should be very freely resorted to.

Diet in convalescence. When the temperature of a simple case has reached the normal, the milk diet may be supplemented by farinaceous foods. In the morning, thin oat-flour porridge with plenty of milk. A little later, a second breakfast of tea and bread and butter. At dinner time, rice and other milk puddings, stewed fruit with plenty of milk, and, if enjoyed, milk soups flavoured with vegetable extracts. In the afternoon, tea with a liberal allowance of milk, bread, butter, and jam. At supper time, bread and milk, or porridge, and a slice of bread, if desired. A pint, at least, of milk, preferably more, should be taken in the twenty-four hours. Water should also be still supplied freely. If febrile complications, such as arthritis or otitis, should occur, this diet may still be given, if the patient has sufficient appetite.

There is no necessity, in my opinion, to increase this dietary until the period at which nephritis most frequently occurs is safely passed.

Exception can be made in the case of adults, fish being allowed from the commencement of the third week. Otherwise it will be withheld till the middle of the fourth, when it may be permitted, as may white meat, rabbit or chicken, meat soups, and a little later meat and eggs. In young children, eight years and under, it will be seldom necessary to give more than white fish. Potatoes may be given at any time in the stage of convalescence, as may fresh fruit. I am far from saying that a more liberal diet may not be given with perfect safety, as, indeed, the practice of many authorities proves, but the above appears to me to be quite sufficient, and is not likely to overtax the kidneys. On the other hand, some recommend diets much more restricted, and many French writers consider that milk, and milk alone, should be allowed. Forchheimer limits the milk diet to the 'nephritic period', the third and fourth weeks of the illness, feeding more liberally in the early stages.

As regards the influence of diet in producing nephritis, different opinions are held. There is certainly little evidence that the occurrence of this complication is in any way influenced by the use or restriction of nitrogenous substances. On the other hand, it would appear only reasonable to put as little tax as possible on the excretory powers of the kidney. Even if a limited diet has no prophylactic effect, it is possible that, when nephritis suddenly supervenes, the lightly-fed patient starts under more favourable conditions than one whose food has not been restricted. But in any case there is no need for being too rigid so far as adolescents and adults are concerned.

Diet in complications. On this question there is little to be said. With the exception of nephritis, the complications liable to occur in the convalescence of the fever demand, as a rule, no modification in diet, unless the pyrexia is considerable and the appetite is lost. In *nephritis*, however the patient may have been fed previously, a milk diet should from the first be insisted on. For a day or two, even, a little arrowroot and water, with no milk, may be given. As long as the urine is restricted in quantity, or hæmaturia persists, it is wiser not to go beyond the milk diet. Fluids must be liberally supplied in order to assist the elimination of waste material by the skin and bowels. A useful drink to give is the so-called 'Imperial drink', which is made by dissolving a drachm of acid tartrate of potash in a pint of boiling water, and flavouring with lemon-juice and sugar. The mixture is allowed to cool before use. Barley-water may also be used. Recently the question of limiting the amount of chlorides given to the patient has been much considered, and, if the food is increased as the complication continues, it is probably wise to restrict the amount of

salt taken. I am not, however, in the habit of adding much to the milk diet, if the amount of albumin remains considerable, unless the condition is prolonged beyond three weeks. If, at that time, albuminuria still persists, the best way to prevent it becoming chronic is undoubtedly to feed. Assuming that the patient has hitherto had nothing more than milk and milk puddings, the addition of one or two lightly-boiled eggs to the day's diet is my first step. Caiger points out that in this way the loss of albumin may be to some extent replaced, and, since trying his method some years ago, I have always used it, being entirely satisfied with the great improvement in the colour and strength of the patients and with the rapid disappearance of the albumin from the urine. It is just at this time, also, that we are accustomed to prescribe iron, and it is probable that the comparative richness in iron, possessed by eggs, may have something to do with the good results obtained.

Local treatment. The condition of the throat plays such an important part in determining the severity of a case, that the greatest attention must be paid to it.

In mild cases in which there is little more than slight congestion it is, I think, wise not to use very active local treatment. The patient if able to do so may use some unirritating gargle, such for instance as listerine, a dessertspoonful to the tumbler of hot water. Or a preparation of a similar nature, containing thymol as its active constituent, may be found cheaper in hospital practice. Swabbing the fauces, and mouth generally, with a mixture of boroglyceride and glycerine, equal parts, or with listerine, or with a solution of chlorate of potash, is useful in younger children. Chlorine water has a deservedly good reputation as a gargle, and we have found eusol also of service in very dirty throats. If there is much cedema and pain the inhalation of steam, medicated or otherwise, at frequent intervals, will give much relief, and hot fomentations applied to the throat have a similar effect. The occurrence of such complications as adenitis, rhinitis, and otitis is undoubtedly influenced by the severity of the throat lesions and by the condition of the mouth. The latter, then, should be kept scrupulously clean, and Hunter recommends the daily swabbing of the mouth and gums with 1-40 carbolic acid to combat any oral sepsis that may be present. Others have recommended the swabbing of the fauces with carbolic and eucalyptus oils.

When the fauces are definitely patched, I still prefer swabbing with antiseptic lotions to either douches or sprays. As a rule the exudation is readily detached and its mechanical removal at frequent intervals will keep the throat satisfactorily clean in most instances, provided the applica-

tions are not of a nature to irritate the mucous membranes, in which case the condition is likely to get worse. Some believe in the daily irrigation of the fauces with hot water from a douche can, which must not be held at such a level above the bed that the pressure is too strong. This is, as a rule, an agreeable and effective way of keeping the throat clean, but I think should be reserved for cases in which the throat is very dirty. I do not use it as a routine in mild cases. Knyvett Gordon recommends that during an irrigation the patient should lie on his stomach, with the head projecting over the edge of the bed, the forehead being supported by the nurse. The whole object is flushing, not antisepsis, and warm water is probably the best thing to use.

How far are we to use *local applications in convalescence*? In hospital, especially in busy wards, it is a question if frequent throat treatment of clean cases is not, in the long run, productive of more harm than good, as the chances of infection from other patients are much increased, however careful the nurses may try to be. But, in private practice, it appears reasonable to continue local treatment throughout the convalescent stage, and, by doing all that is possible to disinfect the throat and nose, to shorten the period of infectivity of the patient.

Treatment of septic cases. In severe or septic cases more energetic treatment is necessary. Douching or syringing either merely with hot water, or with peroxide of hydrogen or chlorine water, should be frequently employed, especially in the early days of the illness. The ulcerated parts should be swabbed freely, and I find Löffler's solution of toluol useful for this purpose (see chapter on diphtheria), provided care is taken not to touch unaffected mucous membrane. Gordon recommends pure izal, undiluted, which, he claims, has a selective action on necrotic tissue and is slightly anæsthetic. In very filthy cases forcible syringing is justifiable, but it is almost certain to assist in the production of otitis, which, after all, is practically inevitable; the syringing, however, cleans the throat very effectively. Sprays of peroxide of hydrogen and perchloride of mercury (1 to 1,000 solution), equal parts, may also be used frequently both for the throat and nose. The treatment must be repeated at short intervals, and it may even be necessary to wake the patient to carry it out. It is of the utmost importance to hold the condition in check so far as possible. While manipulations are in progress, the child should be rolled up in a blanket and immobilized. It is a good plan to use poroplastic splints for the arms should the irritating nasal discharge cause him to pick at his face.

We have already seen that attention to the throat and nose is of primary importance. As regards general management we have to recollect that two

main difficulties stand in the way of effective treatment. Firstly, the patient is restless and sleeps badly and becomes early worn out in consequence. Secondly, he is difficult to feed, the painful condition of his throat interfering with swallowing, and the appetite being completely lost owing to fever and toxæmia. When I can, then, I always put such cases out in the open air, and in any case try to nurse them in open-air conditions. The result is sometimes extremely good, the patient resting well, and often acquiring some desire for food. When, however, swallowing is extremely difficult, nasal feeding must be resorted to, and the fauces are all the better for escaping, in this manner, from the irritation caused by the lodgement of particles of food (see above, dietetic treatment).

Alcoholic stimulation is usually necessary in septic cases. It may be supplemented by such drugs as strychnine and strophanthus. The former of these is particularly valuable if there is any broncho-pneumonia present. Occasionally in very severe cases the intravenous injection of saline solution appears to do good. If the patient is not taking a sufficiency of fluids, hypodermic injections of saline, or large saline injections by the bowel, are, in any case, most useful. It is seldom necessary to interfere with the course of the temperature by other than hydrotherapeutic measures, and of these frequent tepid spongings are the most satisfactory. If plenty of fresh air fails to secure sleep I believe in a dose of hot whisky toddy at night, given just after a cool sponge. If this is not sufficient, many children take small doses of bromidia very well. In hospital, septic cases should be as far as possible isolated. If this cannot be arranged, special rules, regarding their throat instruments and their crockery, must be laid down. In some hospitals the nurses attending to them wear rubber gloves. Provided the greatest care is taken in disinfecting the gloves afterwards, this practice is theoretically a very sound one. But anything short of boiling them between each case cannot be regarded as absolutely safe.

Treatment of toxic cases. This is, in most instances, quite hopeless. Nevertheless everything possible must be tried. Free stimulation, preferably with brandy, is the first essential. This not only improves the circulation, but, at the same time, may assist in procuring the action of the skin, which is so greatly to be desired. I firmly believe that, if a good skin reaction can be obtained, the patient lives longer and has a better chance of recovery. For this reason packing with hot bottles and blankets, mustard fomentations, and two or three drachms of liquor ammoniæ acetatis are usually my first step. Secondly, with a view of assisting elimination of toxins and diluting the poisonous blood, intravenous injection of a pint to two pints of normal saline is always worth trying. I have seen two patients, who were

typically 'malignant', recover under this treatment. In both the skin suddenly began to act freely shortly after an injection. Should the state of the pulse allow it, anything from 4 to 10 oz. of blood may be abstracted from the vein before the saline is injected. Hyperpyrexia, as indicated above, is best controlled by the application of ice to the head. Hypodermics of strychnine or camphor may be given at frequent intervals.

Although we naturally regard with distrust the use of a particular remedy because it has been found specific for another disease, the employment of salvarsan and neo-salvarsan in severe cases of scarlet fever might be justified on the supposition that the etiological micro-organism of the disease may possibly be protozoal in nature. In any case the severe necrotic condition of the throat is not infrequently associated with the spirochætes of Vincent. I have had no experience of the remedy, and its results in scarlet fever do not, in the meantime, appear to be very convincing.

Serum and vaccine treatment. It is for toxic and septic cases that serum has been most frequently employed. To admit that it can really influence a toxic case we must accept the view that scarlatina is primarily a streptococcal infection, an assumption which is being more and more discredited by modern research. The serums used are bactericidal preparations derived from animals immunized against streptococci procured from serious cases of scarlatina and also from different streptococcal infections. These polyvalent serums are given in the hope that one at least of the strains of micro-organisms employed will be the same as that responsible for the patient's infection. I have made no use of them for purely toxic cases, but Knyvett Gordon considers that they may be used with great advantage for that type of the fever. There is, however, much more to be said for their employment in septic cases, although in my own hands it has been as a rule most disappointing. Occasionally an almost miraculous recovery occurs, and it would appear that in such a case the serum has been prepared from a strain of streptococci identical with that causing the worst features of the illness. But in most instances any improvement which may follow its injection might be perfectly well accounted for on other grounds, and in many cases no improvement is observed at all. If it is used, large doses—50 c.c. for instance—are necessary, and should be repeated if required. I cannot say that I have observed any ill effects follow its use, and it may well be given in a bad septic case on the chance of its success or while autogenous vaccines are being prepared. A combination of serum and vaccine treatment, indeed, is recommended by Jochmann, and I have occasionally seen it followed by good results.

The most successful serum appears to be that of Moser. I have had no

opportunity of trying it, but it is regarded by Escherich and Schick as the only treatment likely to influence severe toxic cases. It is prepared from strains of streptococci derived from the blood of cases fatal in the first three days of illness, and injected in living bouillon cultures into horses. The curious fact about it is that in its action it seems to be antitoxic rather than bactericidal, and it does not appear to be very successful in improving the throat-lesions of septic cases. Its apparent success in the toxic type of the fever has been used as an argument for the streptococcal origin of scarlet fever, but it is well to remember that its value as a therapeutic agent has been questioned by competent observers. The dose recommended is 200 c.c., and serum sequelæ are said to be frequent and severe.

The *serum of convalescent patients* has also been employed for therapeutic purposes by Leyden and, amongst others, more recently by Koch, who recommends doses of 100 c.c. The difficulties of procuring such a serum are obvious and, although some degree of success has been attained by its use, its value has been differently judged. A theoretical objection might be raised by those who hold Schick's theory of scarlatinal complications, for the injection of a serum taken, as is Koch's, from patients from eighteen to twenty-four days ill would be liable to set up a condition of passive anaphylaxis.

Interesting work on this treatment with convalescent serum has been recently done in the United States. Zingher, in particular, has done much to simplify the technique by the use of 'whole blood'. This has the advantage that there is much less waste of serum. The injection, of course, cannot be intravenous, but encouraging results have been obtained by intramuscular injection. The procedure is to draw from the convalescent donor a syringe-full of blood and, leaving the needle in the vein, to inject it promptly into the muscles of the patient. An assistant is detailed to attach to the needle, which is left in the arm of the donor, a smaller (5 c.c.) syringe containing a 1 per cent. solution of sodium citrate and, while the injection is proceeding, to so manipulate it as to keep the needle patent. The injection having been completed, the operator returns with the original syringe and refills it, returning to the patient to inject its contents into another muscle. This process may be repeated several times, if desired, and if necessary the syringe can be rapidly rinsed in a beaker, containing citrate solution, between the injections. Amounts up to 250 c.c. have been given in this manner. One dose appears to be sufficient.

Zingher finds this method gives good results which follow almost immediately in toxic cases but which are not so striking in patients of the septic type. The latter indeed improve, but show a similar improvement with

normal blood. I have only treated two cases by this method (Fig. 20). The first was undoubtedly a genuine toxic case and, in the opinion of all who saw her, death appeared certain. From the moment of injection the tem-

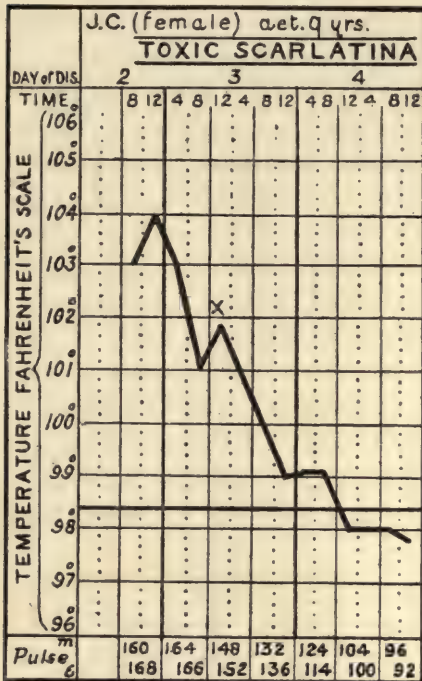


FIG. 20. A case of toxic scarlet fever treated by Zingher's method of injection of 'whole' convalescent blood. The cross indicates the intramuscular injection of 45 c.c. of blood taken from a convalescent donor whose illness commenced 24 days before. The patient, whose chart scarcely indicates the severity of the attack, was cyanosed and in a condition of restless delirium. The pulse was very small and soft and she appeared moribund. The improvement was continuous from the moment of injection, and in 36 hours she was out of danger. We have since treated another similar case by this method with an equally good result.

perature and pulse steadily declined, the cyanosis diminished, and the general condition improved. It is of course possible that this was a coincidence, but the course of the case so closely resembled that of those published by Zingher, and was so unlike that of any other case in my experience, that I am inclined to believe that the patient owed her life to the injection, and I propose to try the treatment again on the first suitable opportunity. Unfortunately toxic cases are not common in Edinburgh, and I fear also there will be difficulty in securing donors at the moment they are wanted. I have only seen two other cases, which I honestly believed to be malignant, recover (see page 145).

Attempts have been made both to prevent and treat the disease by means of streptococcal vaccines. So far as my own experience goes, treatment by vaccines is somewhat disappointing. The prolonged course of cases of the septic type of the fever nevertheless suggests that, if an efficient vaccine could be procured, the condition is one suited for this method of treatment. I do not remember obtaining satisfactory results from the use of stock streptococcal vaccines. On the comparatively few occasions on which the treatment has appeared

to influence the course of the illness favourably, an autogenous vaccine has been used. Again, the vaccines which I have had prepared from the patients' own micro-organisms have not been exclusively streptococcal. In

the type of septic case with which we have had to deal in Edinburgh lately, staphylococci sometimes appear to predominate, and an appropriate vaccine is used. Not infrequently, with a view of saving the time required to obtain pure cultures, a mixed vaccine of the predominant micro-organisms has been used, and I am by no means certain that this haphazard method has not been attended with the best results. A dose of 50 or 60 millions of killed germs, followed at intervals of five or six days by smaller amounts, is what I have usually prescribed, but it is possible increasing doses might have given better results. I have never had the impression that the vaccines did any harm to the patient, and, that being so, employ them in the worst septic cases when possible, but have not had sufficiently striking results to be able to recommend them with any confidence. As is the case with serum, it is almost impossible to estimate the value of a treatment restricted to small numbers of selected cases which may be much more, or much less, virulent than apparently similar cases regarded as controls.

MANAGEMENT OF CONVALESCENCE AND TREATMENT OF COMPLICATIONS. We have seen that it is perhaps wisest to keep the patient in bed for three weeks. We cannot by this procedure hope to avert complications, but, should they supervene, it is just as well that they should find him in bed. After the acute stage is over a careful watch should be kept upon the temperature, the urine, and the appearance of the patient. Any rise of temperature must be carefully investigated. It is often readily explained by the presence of pain in the joints or in the ear, or the glands may be obviously enlarged. Even when pain in the ear is not complained of, and the child seems perfectly well, otorrhœa may appear in a day or two and the pyrexia subsides. Sometimes a very small gland is sufficient to cause a considerable amount of fever of a remittent type, the morning readings being often normal. Again, a rise of temperature may be the first sign of nephritis. When no obvious explanation is found the heart should be carefully examined. Slight degrees of endocarditis seem sometimes to be responsible for an otherwise unexplained pyrexia. The urine should be examined at least every second day throughout convalescence, and it is a wise precaution to test it daily from the sixteenth to the twenty-sixth days. As regards the patient's appearance, any alteration of it should excite attention, and sometimes slight puffiness may be an early sign of nephritis, or the projection forwards of an ear the first indication of mastoid trouble. Edema, indeed, is sometimes, if rarely, noticed a day or two before any change can be detected in the urine. If a patient vomits, the urine should be examined *at once* and, should albumin be found to be present, appropriate treatment started without delay.

Nephritis. As soon as albumin appears in the urine, even if there are no signs of acute nephritis, it is safer to treat the condition seriously, although Escherich and Schick state that untreated patients often appear to do quite well provided that they are suitably dieted and kept in bed. The patient should be put between blankets, and several hot-water bottles placed in the bed. The urine passed should be carefully measured and, if it is found deficient in quantity, it will be necessary to secure free action of the skin and bowels as long as the condition lasts. In any case the patient should receive a purge, say jalap 30 to 60 grains, as soon as the albumin appears, and if the urine is at all scanty this may be repeated nightly. If the initial symptoms are acute, with a rise of temperature, a high tension pulse, and a dry skin, a hot pack should be given at once, and as soon as perspiration is free it can be adequately maintained by the blankets and hot bottles in the bed. For a pack a blanket should be wrung out of very hot water and the patient wrapped in it with a dry blanket, or waterproof sheet, over all, and three hot bottles on each side. This is often very effective, perspiration sometimes breaking out on the face in a few minutes. Another good treatment is the hot-air bath, which can be given by means of a cradle supporting the bedclothes, and a lamp burning under an old croup kettle, with the bottom knocked out, at the foot of the bed, the spout of the kettle carrying the hot air under the bedclothes. Or electric lamps may be fixed to the cradle, as recommended by Goodall and others. A vapour bath from an ordinary croup kettle is also sometimes effective. For patients with high temperature, a small pulse, cyanosis, and signs of cardiac dilatation, Baginsky speaks very highly of a *cold* pack, this being surrounded with blankets and allowed to continue for some hours until, in fact, it becomes a hot one and induces sweating. This method appears worthy of a trial, and is said to be particularly efficacious if there is much restlessness. Drugs to secure an action of the skin are often disappointing, but I have some faith in large doses of liquor ammoniæ acetatis by the rectum. Pilocarpine is very dangerous, and, so far as my experience of it goes, appears to cause œdema of the lungs.

The main point is undoubtedly to see that the patient sweats. As regards the kidneys, poultices and fomentations over the loins are perhaps useful, and either dry or wet cupping may be employed in sharp cases with complete suppression. I do not believe much in diuretics, though at one time I used to give citrate of potash for this purpose. If anything is to be used, digitalis, which is often also useful for the heart, is much to be preferred. Plenty of water and diluent drinks by the mouth are usually quite sufficient, and if continuous vomiting does not allow of this administration, water

can be supplied per rectum. To assist excretion in every way, I usually wash out the bowel with a large irrigation of hot water daily.

Should convulsions occur, and not be relieved by hot packing, a few whiffs of chloroform often give much relief, but, if the circumstances allow of it, it is always worth while to try venesection, and to abstract from 4 to 10 oz. of blood according to age. This sometimes acts like a charm. The same treatment is applicable to coma, but when a patient has once become profoundly unconscious therapeutic measures are usually of little avail.

The amount of urine passed daily must be watched throughout and, as more urine is passed and albumin becomes less, the heat of the bed may be reduced by removing one or more hot bottles. The dietetic treatment of nephritis is important, and has been described on a previous page (see p. 142).

Arthritis may be treated on general principles. The affected joints should be wrapped up in cotton wool and the patient placed between blankets. It is always good practice to try salicylate of soda, which I usually combine with bicarbonate of soda, but too much disappointment need not be felt if it fails to relieve the pain. I do not think that the drug is nearly so effective as it is in acute rheumatism. Aspirin, if preferred, may be employed. For very painful joints I often use the oil of winter-green (salicylate of methyl) applied locally on a piece of lint. The sickly smell of this preparation, however, renders it somewhat unsuited for hospitals, where the feelings of other patients may have to be considered. As a rule the condition is short-lived and it is difficult to estimate the value of any remedy, as, even when untreated, symptoms may altogether disappear in three or four days.

Adenitis may be treated by fomentations of 1-80 carbolic acid frequently applied to the neck, or the part may merely be covered with cotton wool. Should suppuration occur the gland must, of course, be opened, but it is well to delay as long as possible and allow the mass to thoroughly break down. Otherwise healing appears to be very slow. If there is marked cellulitis of the neck there is little advantage in making incisions as long as the mass remains hard. The wounds always slough, and little or no relief is given. It is therefore wiser to wait.

Otorrhœa is always a troublesome complication. The ears should be kept scrupulously clean and frequently syringed. Boracic lotion is probably the most satisfactory preparation to employ. The practice at the City Hospital is to instil a few drops of peroxide of hydrogen into the affected ear, and, after leaving it for about ten minutes, wash out with warm boracic lotion, without using too much pressure of the syringe. The meatus is

then carefully dried with a little cotton-wool twisted on a wooden match, lightly plugged with sublimated cotton-wool, and covered with a pad and bandage. In bad cases this should be repeated every four or six hours. I have occasionally used urotropine internally but without marked results, and vaccines, made from the organisms cultivated from the discharge, have also been disappointing. Should any redness, tenderness, or fluctuation appear behind the auricle, or should there be œdema extending forward over the zygoma, the periosteum over the mastoid is divided at once, and we find that seldom is anything further necessary. Hot fomentations are always applied in these cases for several days after the incision is made. The wound usually heals well. If there is any exfoliated or carious bone found on incision I am accustomed to call in the aid of an aural surgeon, but, provided there has not been too much delay, dead bone is seldom found when the periosteum is divided. In the event of acute symptoms, fever and the like, occurring, either mastoidectomy or the radical mastoid operation may be necessary. Some, indeed, recommend that the first of these, at least, should be performed if a discharge from the ear lasts for more than six weeks. But many consider that it is quite safe to allow an ear to discharge for ten weeks before interference is necessary, and it will be found that in few cases does the otorrhœa persist so long.

Those who believe in early operative interference justify their procedure by pointing out the risks incurred by a patient whose ear continues to discharge. It is said that such persons are living on the brink of a precipice and that serious mastoid or cerebral trouble may occur at any moment. In my own view such an assertion, however just theoretically, is not entirely borne out in practice, and I cannot help feeling that the recuperative powers of young children are underestimated. A very small percentage of the otorrhœa cases leave hospital before the discharge has ceased, the custom being to detain them for twelve or fourteen weeks from the commencement of their fever, should the otorrhœa persist. After that time most ears are quite dry, and my experience coincides with that of Goodall, that deafness is most uncommon. Should, however, the patient be deaf, or should discharge be present when the patient leaves the hospital, the attention of the medical attendant is drawn to the condition, or the parents are advised to consult an aural surgeon should the discharge still continue.

I would recommend, then, that operation be delayed until acute symptoms arise, or until a discharge has persisted for, at least, eight or ten weeks. In such cases the assistance of an expert should be sought. It is true operation may have one advantage, that of stopping a possibly infectious discharge. But in a recent report of Matthews (see p. 606) it is made clear

that the percentage of infecting cases causing 'returns' is as low for patients suffering from otorrhœa as for those in whom no such discharge exists, and it is doubtful if operation, as a public health measure, can be justified.

As regards treatment before the discharge from the ear is established, this is often impossible, for, as we have seen, the otorrhœa is frequently the first symptom that anything is wrong. There is something to be said for incising the tympanum in adults who may be suffering great pain, but in the small children who are the most frequent sufferers it is very difficult to make an adequate examination owing to their pain and struggling. Hot fomentations often give relief in such cases.

Little can be done to prevent the occurrence of otorrhœa, although its frequency appears to have diminished since more attention has been paid to the isolation of septic cases. Our present routine is to have the ears of every patient thoroughly syringed on admission, and thereafter treated thrice daily for ten days with drops of boric alcohol (a saturated solution of boracic acid in 40 per cent. alcohol), a little cottonwool being placed in the meatus afterwards. Should discharge occur it is much less likely to be infected by extraneous micro-organisms, and after five years experience of this method I am inclined to think we have fewer bad cases of otorrhœa. It would be a very great advance if every fever hospital could have an expert otologist on its staff.

Rhinitis is perhaps the most troublesome of all the sequelæ of scarlatina and is extremely intractable. The nose should be syringed, douched, or sprayed at frequent intervals, and a mixture of peroxide of hydrogen and 1-1,000 corrosive lotion is suitable for the purpose. I have for some years been accustomed to give a small dose, 1,500 units, of antitoxin on the assumption that the diphtheria bacillus is responsible, and if this injection is made on the first day of the discharge it is surprising how quickly it clears up in many instances. In prolonged cases I have often fancied that a few drops of a solution of protargol instilled into the nostrils twice daily has had a good effect. A small plug of carbolyzed vaseline in each nostril at night is also useful, and serves to prevent the excoriation so often noticed at the orifices.

Other complications must be treated on ordinary lines.

PROPHYLAXIS. It is nowadays customary to treat most cases of scarlatina in hospital. The advantages and disadvantages of this method, and the duration of infectivity, are discussed in the last chapter of this volume. Isolation can in some cases be carried out quite effectively at home. The disinfection of fomites and of infected houses is possibly important, the scarlatinal virus being long lived. The patient should be

kept isolated as long as any discharge from the nose, ear, vagina, or suppurating wound persists. While late desquamation may be disregarded, a detention of five weeks from the first day of illness is probably advisable, particularly for children. Susceptible contacts should be quarantined for seven days, before being allowed to mix with other children in school or elsewhere. This interval exceeds by an adequate margin the longest possible period of incubation.

When an outbreak occurs, the milk supply should always be investigated, and all cases of sore throat occurring among children should be carefully watched. There is reason to believe that mild unrecognized cases play a great part in disseminating the infection. It is also worth remembering that cases occurring at long intervals in the same house may be accounted for by the fact that the original patient, though apparently quite well, still harbours the micro-organisms responsible for the disease, and is 'intermittently infectious', the infection being lit up, as it were, at varying intervals.

CHAPTER V

SMALL-POX

Introduction.	Period of Convalescence and Desquamation.
Etiology : the 'cytoryctes variolæ'.	Complications and Sequelæ.
Dissemination : susceptibility, predisposing factors.	Types : varioloid, toxic or hæmorrhagic.
Period of Incubation.	Small-pox and Pregnancy.
Period of Invasion : the initial fever, prodromal rashes.	Second Attacks.
Period of Eruption : the papule, distribution, the vesicle, the pustule, desiccation, pitting.	The Blood in Small-pox.
Classification of Eruptions : discrete, coherent, confluent.	Morbid Anatomy.
Symptoms of the Secondary Fever.	Diagnosis : of initial fever, of eruption.
	Prognosis : vaccination, severe symptoms, &c.
	Treatment : general, local.
	Prophylaxis : isolation, vaccination, quarantine, disinfection, &c.
	Hospital 'influence' : aerial convection.

Synonym—Variola. *French*, Petite Vérole. *German*, Blattern.

INTRODUCTION. It is a subject for legitimate regret that a textbook on fevers, written a century after the introduction of vaccination, should still have to include an account of a disease which should long ago have been classed with such conditions as the 'Sweating Sickness', or the 'Black Death', and relegated rather to historical treatises. It is an interesting and curious comment on our boasted civilization that, with the means of absolutely preventing small-pox at our disposal, we allow the prejudices of a small minority still to expose the country to not infrequent outbreaks of a peculiarly repulsive and filthy disease. But unfortunately, so long as vaccination and revaccination cannot be universally enforced, small-pox will continue to be with us, and, unfortunately also, will continue to be the cause of most regrettable loss of life and waste of money. It is true we have much to be thankful for. The great epidemics of the old days are no longer possible. But our comparative immunity from the disease has become in itself a source of risk, as there are many medical men in practice who have never seen a case of small-pox, and who, therefore, are liable to fail to recognize it when it occurs. And as it is of the greatest importance that a first case should be isolated at the earliest possible

moment, and all precautions promptly taken, the careful study of the appearances presented by this fever are of the greatest importance.

ETIOLOGY. It is practically certain that small-pox, like other acute infectious disorders, is caused by a living micro-organism, and there is some reason to believe that it will be found to be very minute, as there is little doubt it will pass through the coarser porcelain filters. Bacteriological research has so far failed to isolate from the pustules any germ which can be regarded as being responsible for the disease, the bacteria discovered being for the most part pyogenic organisms which may doubtless play an important part in the production of the secondary fever, but which probably have no connexion with the original infection. Recently Rabinowitsch has described a small organism which he has termed a strepto-diplococcus, and which he has recovered from the pustules, spleen, and bone-marrow of small-pox patients. This germ in pure culture causes, when inoculated into the skin of small animals, lesions identical with those produced by the inoculation of pustule-contents or of vaccine lymph, but it has not so far been proved to cause typical vesicles in the calf. Rabinowitsch regards it as identical with the '*Microsoma Variolæ*' described by Fornet, but the latter considers that there are well-marked differences. While bacteriological work undertaken in recent years is free from many of the objections and fallacies of that of earlier workers, it would be premature to assume that the cause of small-pox is bacterial in nature. It appears somewhat more probable that it will be found to be protozoal. Guarnieri in 1892 first gave the name of the *Cytoryctes Variolæ* to the so-called vaccine bodies, the presence of which in vaccine and variola vesicles, and in the lesions caused by inoculation of the cornea with vaccine or variola virus, had already been noted by various observers. Later, Wasielewski confirmed the work of Guarnieri and concluded that the vaccine bodies are the only characteristic structures which can be found in the skin and mucous membrane in variola and vaccinia, and that they can only be produced in the epithelial cells of a rabbit's cornea by inoculations with vaccine or variolous matter. In 1904 Councilman, who made an elaborate study of the histology of the skin in small-pox, came to the conclusion that the vaccine bodies, which he described as minute rounded refractive forms in the cells, were in reality a phase in the life history of a sporozoon. His work, however, has remained unconfirmed. Prowazek, indeed, states definitely that the bodies are not protozoal in nature, but considers they may be due to nuclear changes due to a specific reaction of the epithelial cells to variola virus. He himself has described other bodies which, he inclines to believe, may be protozoa, and other observers claim to have seen spirochætes. Proescher, more

recently, reports the presence of intracellular and intranuclear micro-organisms which he has not succeeded in cultivating. These assume both coecal and bacillary shapes, but whether they are the same as those which Rabinowitsch considers to be the causative micro-organism it is difficult to say. We can only conclude that in the meantime nothing really definite is known on the subject.

DISSEMINATION. Small-pox is spread chiefly by *direct infection* from person to person. The patient is infectious throughout the whole course of the disease, from the moment of the first symptoms till the separation of the last crusts from the skin, but is probably most dangerous to others during the stages of pustulation and desiccation. Actual contact is not necessary to contract infection. To enter the room in which a patient is lying, especially if the ventilation is inadequate, appears to be quite sufficient. It is probable that the virus is inhaled. It retains its infectivity for some time in clothing, bedding, and other *fomites*. A recent outbreak in the north of England is said to have been caused by imported Mexican cotton, and, although in this and similar cases which have been reported it is impossible to prove that such fomites are in reality responsible, the presumption in favour of such a view seems fairly strong. The virus can probably be carried some distance by *air*. How great this distance may be is a matter of some contention, and will be discussed in a subsequent page when the prophylaxis of the disease is considered. It is only reasonable also to suppose that the contagion may be carried by *insects*, such as flies. It is beyond question that it is not infrequently conveyed on the clothes or in the hair of healthy *third persons*. Lastly, the disease may be transmitted in a somewhat modified form by direct *inoculation*.

As regards **susceptibility** to the disease, *sex* appears to exert no influence. The same may be said of *age*, always presuming the introduction of small-pox into an absolutely unprotected community, for under such circumstances all ages appear equally liable to an attack of the disease. In the pre-vaccination times the chief sufferers were young children. The disease was as prevalent as measles is to-day, and few persons escaped taking it in the first few years of life, just as is the case with the less dangerous infection. Those who survived were, of course, protected, and the age incidence therefore remained low. But, since vaccination in infancy has become fairly general, the whole situation has changed, and, when an outbreak occurs, the hospitals are filled with adults, children with the disease being comparatively rarely seen, except in those towns which are noted for their contempt of vaccination. Susceptibility is undoubtedly affected by *race*, coloured people generally, and negroes in particular, appearing to be unduly sensitive to the

virus. **Immunity** seems sometimes to be natural, that is to say, modified attacks are occasionally seen in persons who are unprotected by any acquired immunity. Vaccination gives complete protection for some years and partial protection afterwards. The same may be said of a previous attack of small-pox, and of inoculated small-pox, the period of complete protection in their case, however, being considerably longer, second attacks of the disease being rare.

Small-pox may occur in any *climate* and has been met with all over the world. It is more prevalent in the tropics than in temperate countries. As regards *season* it is essentially a disease of winter and spring, epidemics showing a marked tendency to abate with the commencement of summer.

PERIOD OF INCUBATION. The latent stage of small-pox usually lasts from ten to fourteen days inclusive. Brownlee, in a table of the incubation periods of forty-six cases, shows that no less than thirty-seven of them are included within these limits. I have always found it extremely difficult to make certain of the period in my small-pox cases, as it is often hard to exclude absolutely the possibility of more than one exposure. But in those few cases in which I satisfied myself that the exposure was limited to a few hours, and was not repeated afterwards, the latent stage has lasted exactly *twelve days*. Most patients probably have an incubation period only slightly longer or shorter than that time. Brownlee gives the extremes at eight and sixteen days respectively. Other observers note periods which show more deviation still. Thus Curschmann reports a case which developed in five days, McCombie one of seven days, and, on the other hand, it has been stated that occasionally the disease may take so much as twenty-three days to develop. It is probable that short incubations are more commonly met with than those which exceed sixteen days. Both, however, may be regarded as extremely rare.

PERIOD OF INVASION AND THE INITIAL FEVER. The *onset* of small-pox is abrupt, the patient being usually taken ill quite suddenly, and being more or less prostrated from the first. The symptoms most frequently noted at this early stage are headache, chills, pain in the back, nausea, and vomiting. The most constant of these symptoms is unquestionably *headache*. In an analysis of the initial features presented by 203 consecutive cases of small-pox, which occurred in different outbreaks, I found severe headache was nearly always present, no less than 90 per cent. of the patients having complained of it from the commencement of the fever. The headache is usually frontal, and is much aggravated on movement. It is not infrequently accompanied by marked sensations of *giddiness*. The next most prominent symptom is *shivering*, which may be merely an uncomfortable feeling of

chilliness, or which, in severe cases, may be very well marked, actual rigors often occurring. Of the series of patients mentioned above, 84 per cent. had more or less shivering. The symptom, therefore, is only slightly less common than headache. A very important and suggestive sign of the onset of small-pox is *backache*, but this does not occur nearly so often as has been suggested, only 54 per cent. of the patients in my series suffering from this symptom. The pain is usually worst across the loins and the sacrum, and not infrequently also affects the back of the thighs. It is often of a most agonizing character, but occasionally the patient complains no more of it than he does of other pains affecting the limbs and trunk. When, however, it is voluntarily complained of, it is of considerable assistance in diagnosis. Nausea is nearly always present to a greater or less degree, and the patient has no desire for food. Actual *vomiting* is more common in children than adults. In my series, however, it occurred in the same percentage of patients as did backache.

In addition to the above group of symptoms, which, considered concurrently when small-pox is epidemic, should always suggest the possibility of the disease, the patient suffers also from all the symptoms which are naturally to be expected in a condition of marked toxæmia associated with high fever. Loss of appetite, loss of sleep, severe thirst, and delirium, often well marked in young or alcoholic subjects, are all noticed. Drowsiness is frequently present, particularly in young children, and even coma may appear at this stage. Convulsions are also occasionally seen in children. The patient is usually much prostrated and looks distinctly ill. His face may be flushed, but is often pale, and the extremities may be cold. The skin is usually dry. The tongue is covered with thick white fur, the breath very offensive, and constipation is almost invariably present. The majority of the above symptoms rapidly subside as the temperature falls with the appearance of the eruption of the disease.

The initial fever. The temperature in the prodromal stage of small-pox is often very high. It runs up rapidly from the appearance of the first symptom and may reach 104° within the first twenty-four hours of the illness (see Figs. 21, 22). On the second day this high level is usually maintained, and, indeed, not infrequently exceeded. The fever shows no abatement until the eruption commences to appear, when it falls, as a rule rapidly. The duration of the invasion stage varies. About two days may be taken to be a fair average, the eruption appearing on the third day. But occasionally the period lasts longer, and it may be the fourth or fifth day of the illness before the initial fever has subsided. During this stage the pulse and respirations are both accelerated in proportion to the height of the temperature.

In young children the pulse may be soft and extremely rapid, and in hæmorrhagic cases a soft, weak, quick pulse is also usual.

Prodromal rashes. The most interesting feature of the initial fever of small-pox is the comparatively frequent occurrence of prodromal rashes. These may be divided into three classes, (i) erythematous, (ii) petechial, and (iii) mixed rashes. To consider first those of the *erythematous* variety, these may be roughly classed as either scarlatiniform, morbilliform, or multiform, and may also be general or local in their distribution. They are most commonly seen on the trunk, and seldom, if ever, definitely invade the face. The

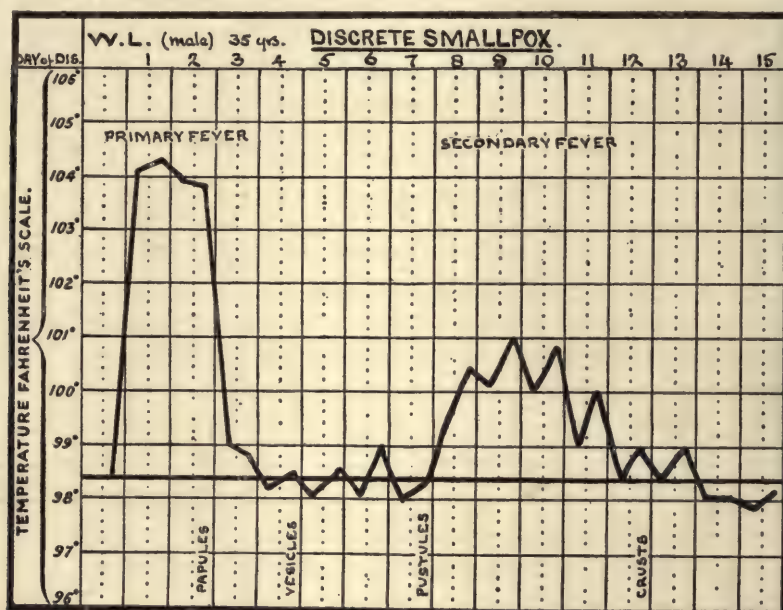


FIG. 21. A case of discrete small-pox from the first day. Slight secondary fever.

limbs, however, are not infrequently affected. Even when distributed all over the body they are apt to be brightest in the inguinal region and in the axillæ. The rashes occur more frequently in adults than in children. It has, in fact, been stated that they do not occur in persons under ten years of age. They may be visible from the moment of the first symptom of the disease, but most frequently make their appearance on the second day. As a rule they are of short duration and vanish when the true eruption appears. They may persist, however, for some days, and are occasionally to be seen even in the late vesicular stage. It is difficult to estimate the frequency with which they occur, as they leave no staining behind them, and, being for the most part short lived, are seldom present on the patient by the time he arrives in

hospital. In my own series of cases I have only been fortunate enough to observe them in 5 per cent. of the whole.

The *scarlatiniform* variety is perhaps the most common. This presents a fairly uniform flush, with some suggestion of indefinite punctation. It is often extremely like the rash of scarlatina, but the mucous membrane of the fauces is not involved. Except in the groins, moreover, it is usually paler in colour than the average scarlet rash. At first sight the *morbilliform* rashes give an admirable imitation of the measles eruption. The macules, however, are larger when they first appear, and they remain macular, not

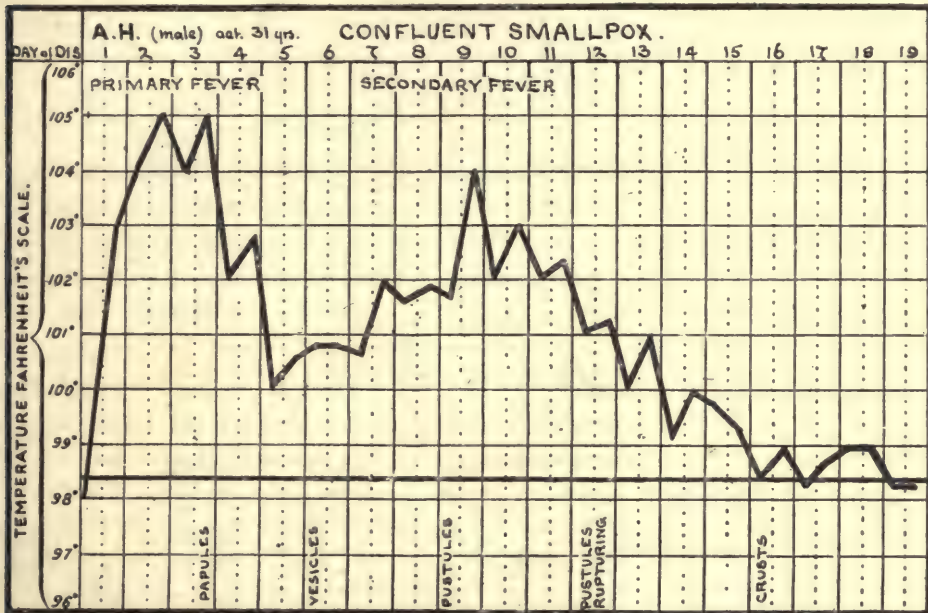


FIG. 22. A severe case of unmodified small-pox (confluent). Note that the temperature does not reach the normal line between the primary and secondary fevers.

becoming raised above the skin. In colour they are quite of the usual measles pink, but are hardly so bright in tint. Here and there crescentic arrangements may be often observed, and it is not uncommon to find the eyes distinctly suffused. There is, however, no catarrh, and, in the examples of this rash which I have personally observed, the face has been quite free from the macules, although the early appearance of the true small-pox eruption on the face, taken in conjunction with the erythema on the body, may suggest the contrary. The rash disappears easily on pressure and fades quickly, leaving no staining. Under the head of *multiform* rashes we may include irregular erythemas, in some parts diffuse, in others measly

or scarlatinal. Urticarial rashes, which have also been described, would also fall in this category.

A very interesting and ill-omened form of erythema, which is sometimes classed as scarlatiniform, but which has distinct characters of its own, is the rash which is called by French authors 'le rash astacoïde', or the lobster rash. This is a very vivid and intense erythema, almost erysipelatous, of a most brilliant red colour, approaching more the tint of scarlet than anything ever seen in scarlet fever. It is general all over the body and involves also the face, which is usually congested and puffy. It only occurs in hæmorrhagic cases, and is therefore of grave prognostic significance. It is early followed by hæmorrhages into the conjunctiva, and later over the surface of the skin.

Petechial rashes are more commonly seen than erythematous ones, as, being stained into the skin, they may be recognized for some time after the true eruption has made its appearance. I have found them present in 9 per cent. of my cases. They consist of small punctate petechial spots, either bright red or deep purple in colour, and either scattered discretely or closely set together in a particular area of skin. They are seen chiefly in two situations, the groin and the axilla, most frequently in the former. In that situation they present the appearance of a *triangular rash*, the base of the triangle being a straight line across the abdomen, usually a little below the umbilicus, the apex in the middle line between the thighs a few inches below the pubes. This situation and arrangement has caused French writers to name the rash the 'bathing drawers rash', as, seen from the front, it includes the region usually covered by that garment. The red and purple petechiæ are usually present together, and are most closely set along the line of Poupert's ligament. They occasionally, if very numerous, coalesce into somewhat larger hæmorrhagic blotches. The rash is liable to appear on the flanks, and a line of petechiæ may connect it with the similar rash which is seen in the axilla. The localization of this prodromal eruption is very interesting. It has been suggested that its distribution depends on the line of nerve terminations associated with the lower part of the spinal cord, and that the intense lumbar pain, so often met with at this period in small-pox, also points to some particular poisoning of this part of the nervous system. But, whatever the cause, the triangular rash is of great diagnostic importance, as it is peculiar to the disease and cannot easily be confused with anything else. Another initial hæmorrhagic rash has been described, consisting of larger purple hæmorrhages, more like those of true purpura, and distributed over the whole body with no particular preference for the inguinal or axillary region.



A



B

SMALLPOX.

A—A prodromal morbilliform rash involving the trunk and to a lesser extent the face. Much of the spotting on the face is due to the first signs of the smallpox eruption.

B—The same patient two days later. The smallpox eruption is becoming vesicular.

The simultaneous occurrence of erythematous and petechial rashes on the same patient is not unusual, and the resulting appearance may be best described as a *mixed* rash. The erythema in such cases is more often local than general, but it is usually more extensive in its distribution than are the petechiæ.

It would appear that the frequency with which prodromal rashes occur varies much in different epidemics. Bancroft, in 1,200 cases, noted them in only sixteen instances, ten of which were examples of the petechial variety. In my own series of cases erythematous, petechial, or petechio-erythematous rashes were present in 14 per cent. of the cases, and it is of course probable that many erythematous rashes had faded before the patients came under observation. In a series of 928 cases Roger and Weil found prodromal rashes present in 22 per cent. of the female and 14 per cent. of the male patients. I have not noticed this difference in the sex incidence. The relation of the rashes to the severity of the cases will be discussed when the question of prognosis is considered below.

We have then the small-pox patient passing through a brief initial fever, accompanied by high temperature, marked prostration, and severe toxic symptoms generally. On the third day, or shortly after it, these symptoms practically disappear with the efflorescence of the true eruption of the disease. Except in hæmorrhagic or confluent types of the illness, the temperature has fallen to normal by the time the eruption is vesicular. Even in the worst cases there is a considerable relaxation of the fever at this time (see Figs. 21, 22, 23).

THE ERUPTION. From this stage onward the history of the small-pox patient, provided the type of his attack is not hæmorrhagic, is the history of his eruption. It is upon the profuseness and development of the pocks that the severity or mildness of his symptoms depend. It will be convenient to describe the stages of this interesting eruption as it is seen in the vast majority of patients who contract the infection in this country, that is to say, in adults who have some degree of protection owing to vaccination in infancy. Any peculiarities which may be observed in unmodified small-pox will be noted afterwards.

The stage of the papule. The first manifestation of the eruption, about forty-eight to sixty hours after the first symptoms of the patient, is the appearance of dull red macules or spots, usually first seen on the brow and wrists. These at first are not raised above the skin, and disappear quite easily on pressure. After a few hours, however, they become distinctly raised, are hard to the touch, and do not disappear completely when the skin is stretched. The macules, then, have become papules. These papules are distinctly harder, more round, and better defined than those met with in

measles. Their colour is darker and they do not show the same tendency to coalesce in groups. When palpated they are in a well-marked case characteristically 'shotty', that is to say, the suggestion to the finger is that of a small shot under the skin. It is well to remember, however, that in modified cases this sign cannot be depended upon. About twenty-four hours after their appearance it is usually possible to see the commencement of vesiculation at the summit of the papules. It is, however, thirty-six or forty-eight hours before the eruption is made up of complete vesicles. During this stage the temperature falls, sometimes rapidly in about twelve hours, often

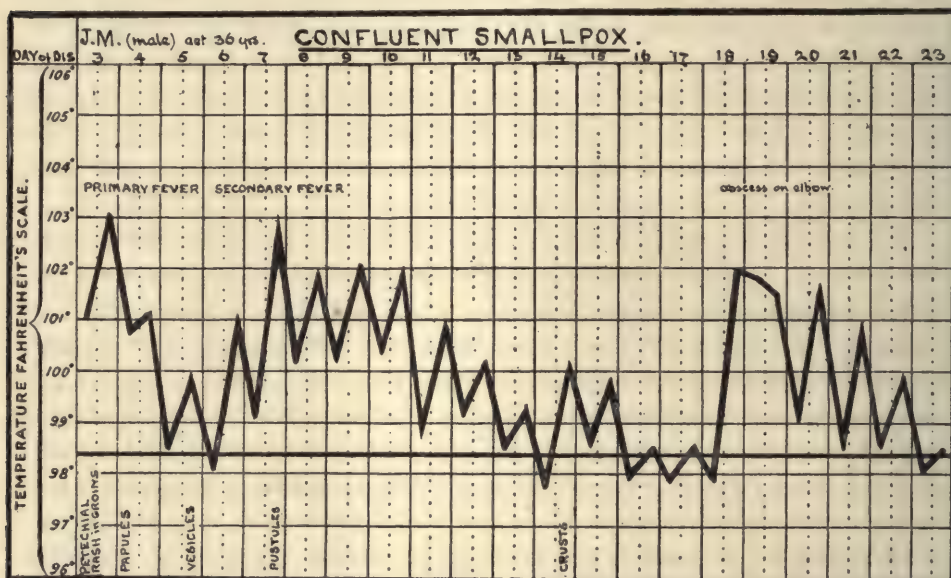


FIG. 23. A case of confluent small-pox of moderate severity, followed by a local abscess.

more slowly, only attaining the normal with the completion of vesiculation (Fig. 23).

The distribution of the eruption. The eruption is general, but shows a marked preference for certain situations. Thus the face and forearms, particularly the wrists, usually bear the brunt of it. The scalp is generally much affected, as is also the back. The upper arms and lower extremities suffer as a rule more moderately. Even in severe cases the chest is often comparatively slightly involved, and the abdomen escapes most cheaply of all. The palms and soles often suffer severely, and the hands and feet generally show a high proportion of lesions. The flexor surfaces are in most cases less severely attacked than the extensor.

With the appearance of the papules on the skin the buccal mucous membranes also become involved, and the palate is often liberally studded with lesions which very rapidly become vesicular and rupture early. The lining membrane of the cheeks, the fauces, and the tongue also show vesicles. The larynx is not infrequently affected, and the eruption may spread down to the bifurcation of the bronchial tubes. Hoarseness and laryngeal symptoms are the result of this involvement of the upper air-passages, and the condition of the mouth and fauces causes great discomfort and often complaint of sore throat. It appears that the œsophagus usually escapes, but Moore has described a case in which the stomach was covered with pocks.

Lesions are frequently seen on the eyelids and more rarely on the conjunctiva. The cornea is not involved unless such a condition as pannus exists previously.

Apart from the special situations which the eruption naturally favours, it is also found to be more profuse in parts where the skin has suffered from pressure, from irritation, and so forth. Thus women may present a large number of lesions round the waist, and, occasionally, the situation of the garter is beautifully emphasized by a band of pocks. Parts of the skin, again, which have been recently poulticed, blistered, or contused, are very apt to show a special concentration, or in sharp cases an actual confluence, of the lesions. In infants, the buttocks, which are liable to excoriation by urine or fæces, are also markedly affected. In patients suffering from old-standing paralysis the affected limb may occasionally be spared by the eruption.

Ricketts, in his valuable work on the 'Diagnosis of Small-pox', which may be recommended to all who take a special interest in the subject, points out how the density of the eruption is throughout influenced by the amount of exposure or irritation to which the skin of the body in various situations is subjected. Thus the protected flexor surfaces suffer less than the extensor, and the flank, perhaps the most protected region of the body, suffers least of all. The prominences of the face, the forehead, malar regions, and nose, show a more profuse eruption than the hollows, the upper part of the face being more affected, in consequence, than the lower. The back of the neck and the projecting lines of the sterno-mastoid present a more dense eruption than less exposed parts. The involvement of the scalp is influenced not a little by the protection afforded by the hair. Bald-headed persons will suffer most in this situation. Arrangement of clothing exercises much influence and accounts for differences observed in the sexes. The distribution of an eruption may largely depend upon the activity of the limbs at the time

the causative material is circulating in the blood. The more activity, the more friction and irritation is probable.

The stage of the vesicle. By the time the papule has become vesicular the patient is usually feeling comparatively well. His temperature is in the neighbourhood of the normal line, his appetite has returned, and, in those cases in which the eruption is very scanty, his troubles are practically over, the secondary fever being dependent on the number of the pocks. The vesicle is at first conical ; its contents are fairly clear and translucent, if not so limpid as is the case in varicella. Its margin is rounded, and is encircled with a distinct areola of redness. It is firmly set in the skin, and is quite hard to the touch in the vast majority of cases. The change from the papule to the vesicle takes place practically synchronously all over the skin, but the lower extremities may at any time during the eruption show lesions at a slightly later stage than the face and upper part of the body. The difference in time in these situations may be sometimes nearly twenty-four hours, the eruption in fact developing earlier in those parts in which it first appeared.

The vesicular stage lasts about four days. During this period the vesicle gets gradually larger, and its contents become more opaque. At first conical it becomes more rounded in outline and shows a central depression or umbilication which may, however, be not present in all the lesions. As the development continues, this depression, which is caused by the centre of the vesicle being held down by the duct of a sweat gland or hair follicle, ultimately disappears, and the whole lesion becomes still more rounded or dome-shaped. By this time the vesicle is the size of a split pea and its contents are becoming milky in appearance, the colour being that of a dull pearl. The vesicle is multilocular, and if a needle is run through it, only a little fluid exudes, and there is no collapse, as is the case in varicella, the shape remaining unaltered. The development of the lesions, if numerous, is by this time sufficient to cause considerable discomfort to the patient, the irritation in the tough skin of the palms and soles being well marked. The temperature is, moreover, apt to rise at night (Fig. 22).

The stage of the pustule. With the change of the character of the contents of the pock into definitely purulent material, the eruption has entered upon its pustular stage. The lesions still increase in size and become more tense. Their colour is now distinctly yellowish. The areola round the pustules becomes more marked and more distinctly red. The inflammatory process, if the eruption is profuse, is accompanied by considerable œdema of the face. As the pustules increase in size the contents of neighbouring ones are apt to become blended together in areas of confluence. The tension in many of the pocks is sufficient to break up the retinaculum which has hitherto



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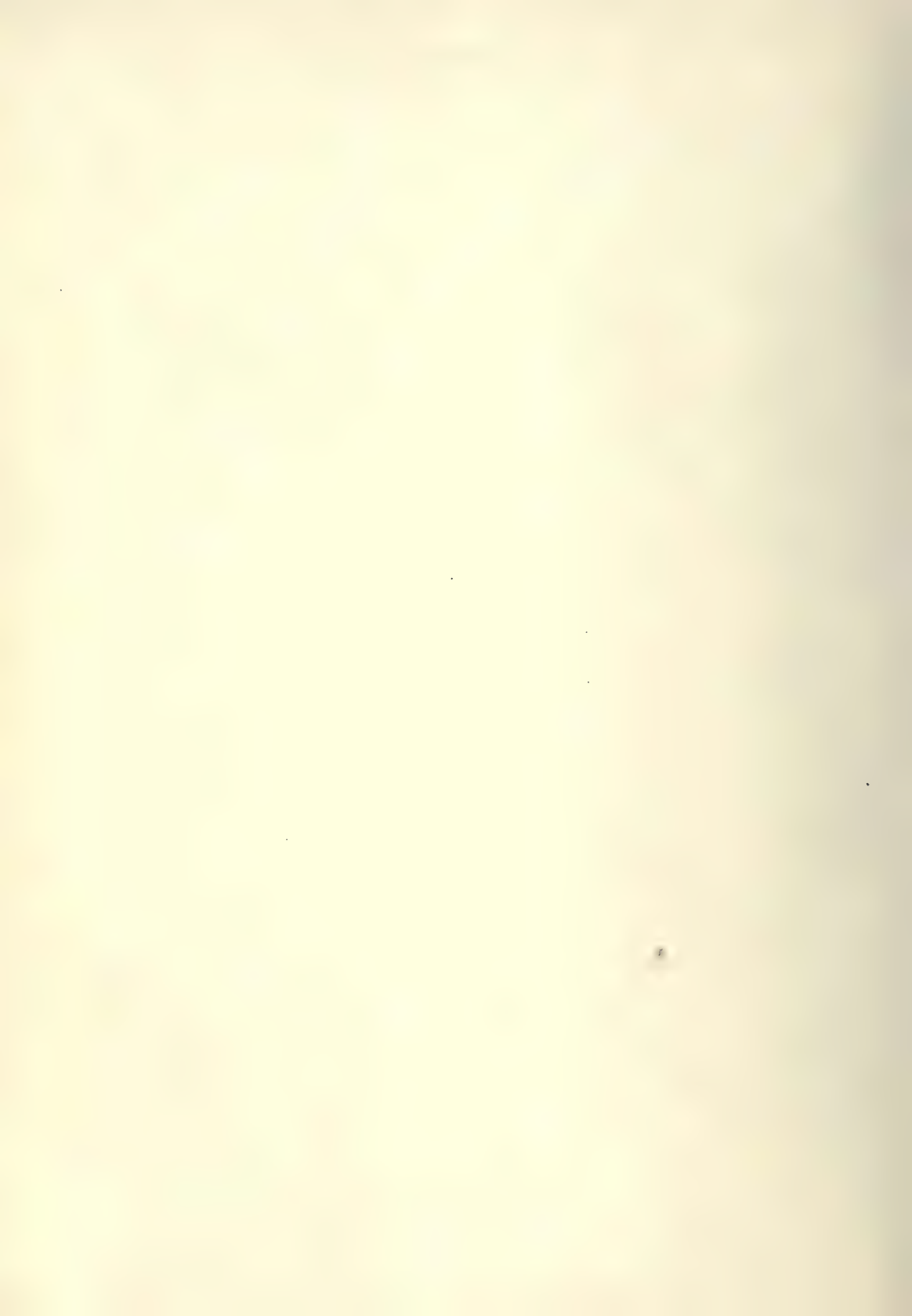


B

SMALLPOX.

A—A confluent smallpox eruption on the extensor aspect of the forearm. Pustular stage.

B—Very profuse discrete smallpox in the pustular stage.



divided them into compartments, and, in the late pustular stage, when the pock is pricked it collapses readily, discharging the whole of its contents. The development or *maturation* of the pustule is accompanied by considerable pyrexia, the so-called secondary fever of small-pox being produced by the process. It is not unusual in severe cases to see large flat bullæ, resembling those met with in pemphigus, on the extremities of the patient.

The stage of desiccation. The period of time occupied by the complete maturation of an average pustule is from three to four days from the time when it ceased to be vesicular. It is now rounded, tense, with little or no umbilication, and with an inflamed and somewhat indurated areola. On the ninth or tenth day of the eruption, the eleventh or twelfth of the disease, the pustules commence to rupture. Some burst from their own tension, discharging thick yellow honey-like material which has a most disgusting odour. Others rupture as the result of accidental pressure, or of the friction of clothes. Some, on the other hand, dry up without having broken. The exuded matter, together with the roof of the ruptured pustule, forms a yellowish brown crust or scab, which may become black from the admixture of blood. The crust, unless deeply set into the skin, owing to the necrotic process having definitely affected the cutis vera, separates easily and quickly, often, indeed, by the thirteenth or fourteenth day of the eruption. If, however, the skin has become much involved, the separation of the crust is a much more tedious matter, and permanent *pitting* or scarring of the skin is left behind. In the case of unruptured pustules, which are most frequently met with in the tough skin of the palms and soles, the dried-up contents gradually shrivel up into a tough brown disc, which lies under the horny layers of the epidermis, and, unless assisted, works its way to the surface very slowly, remaining, as it were, buried for many weeks.

Classification of Eruptions. As, broadly speaking, the severity of an attack of small-pox is in direct proportion to the amount of the eruption, it is usual for the sake of convenience to classify cases under three headings according to the number of lesions which they present. Putting on one side those cases in which the symptoms are altogether so modified that the eruption does not run the usual course, the mildest examples of definite small-pox, in which the pocks, whether few or numerous, are arranged discretely and show no tendency to run together, are classed as *discrete*. More severe cases, in which the pocks, while remaining separate from each other, are so closely set as to leave little or no healthy skin visible between them, are named *coherent* or *semi-confluent*. The worst cases of all, in which the pocks in certain areas have amalgamated and mingled their contents, presenting large patches in which the individuality of the lesions is

completely lost, are termed *confluent*. It must, however, be remembered that this classification depends on the appearance presented by the face and forearms, on which the eruption is always most profuse. Even in confluent cases the eruption on the trunk remains, as a rule, discrete, or only presents small areas of confluence. In some hospitals it is customary to classify the cases by the actual number of the lesions which can be counted on the face. This is no doubt a more accurate method when it is desired to ascertain the effect of vaccination in infancy on the severity of the disease contracted in later life.

Unmodified small-pox is distinguished from the type described above in being, as a rule, slower in its development, and more regular in its evolution. The vesicular stage does not develop so quickly and lasts longer, and the maturation of the pock is also slower. The pocks themselves seem often more deeply set in the skin, and as a result the remission of temperature during the vesicular stage is, even in discrete cases, hardly so complete. The secondary fever is, in proportion to the amount of lesions, considerably more severe. On the other hand, patients who show fairly good vaccination marks, if the disease is taken relatively late in life, have often very severe attacks in which these features are noticed.

THE SECONDARY FEVER. We must now return and follow the patient through the course of his eruption, noting the symptoms which he may present. As has been said above, during the stage of the vesicle he suffers little, only complaining of heat and irritation in the skin. With the appearance of the pustule, however, the *pyrexia* again commences (see Fig 21). It may be extremely slight, lasting only two or three days, and in some cases it is absent altogether, that is if the eruption is very scanty. The average well-marked discrete case, however, will have a fever of from three to seven days, rising to a maximum of about 102° F. In semiconfluent and confluent cases the temperature is more marked and may last from a week to a fortnight, readings of 103° to 104° being not uncommon (Figs. 22, 23), while in very severe or fatal cases the latter figure may be much exceeded. The fever would appear to depend partly on the tension in the pocks and the extreme irritation and discomfort which they cause, and partly, no doubt, upon septic absorption from their contents and from the necrotic areas left after their rupture. The mere rupturing of the pocks in a bad case by no means terminates the fever, which continues during the early stages of desiccation. The *appearance* of the patient is very characteristic. Once a fairly typical case of small-pox has been seen, the picture presented by it is never forgotten—the swollen puffy face with œdematous eyelids, the numerous or scattered pocks, all of a similar size and colour, and presenting no differences, the loose-

lipped mouth, often held half open owing to œdema of the buccal membranes, and the curiously apathetic expression so unlike what would be naturally expected from a patient in such a condition, all tend to leave an indelible impression on the mind of the observer. Later in the disease, if the eruption should have become confluent, the face may appear to be covered by a dirty yellow mask. The features are indistinguishable, the eyes closed. When desiccation has commenced, the face is covered with black and yellow crusts, and glazed with the sticky material which has exuded from the ruptured pustules. Occasionally hæmorrhage has taken place into a certain number of the lesions, giving them a dirty blue or dark purple colour, and suggesting that the patient is much worse than he really is, such an occurrence being of little prognostic significance.

The suffering caused by the condition of the skin is often intense. At first heat and irritation only are complained of. Later there is much soreness and sometimes great pain. The weight of the bed-clothes and the pressure of the body on the mattress are often a source of great distress. The stiffness of the hands and fingers, which cannot be moved and are usually held partly flexed, is another cause of discomfort. Pustules in the eyelids are extremely painful, the mouth is usually very sore and uncomfortable, and the tongue often much swollen. Some patients are themselves acutely conscious of the sickening and fetid odour of their skin, and this adds much to their distress. When the crusting process has begun, the itching, which becomes marked at this time, is almost intolerable.

Insomnia is a frequent symptom, as is only to be expected. It may be present in the vesicular stage, but usually gives most trouble during the maturation of the pock. There is also not infrequently some *delirium*. Some patients become wildly excited and, unless carefully watched, are very apt to get out of bed. As the disease advances, bad cases drift into the *typhoid state*, lying helplessly on the back, with low muttering delirium, subsultus of the tendons, and picking at the bedclothes. All these symptoms may

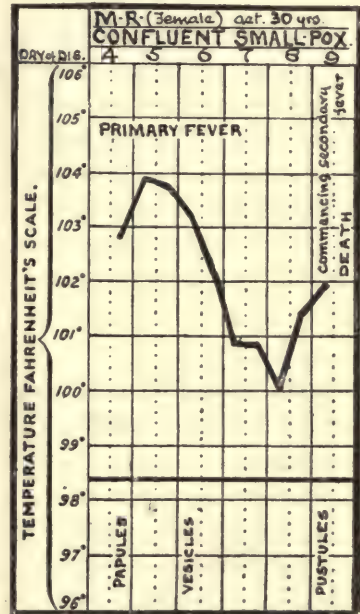


FIG. 24. A very severe case of confluent small-pox (unmodified), with only slight remission of temperature and early death.

happily pass off and the patient recover. Should *death* occur, it may be preceded by hyperpyrexia. The most fatal days are the twelfth, thirteenth, and fourteenth of the disease.

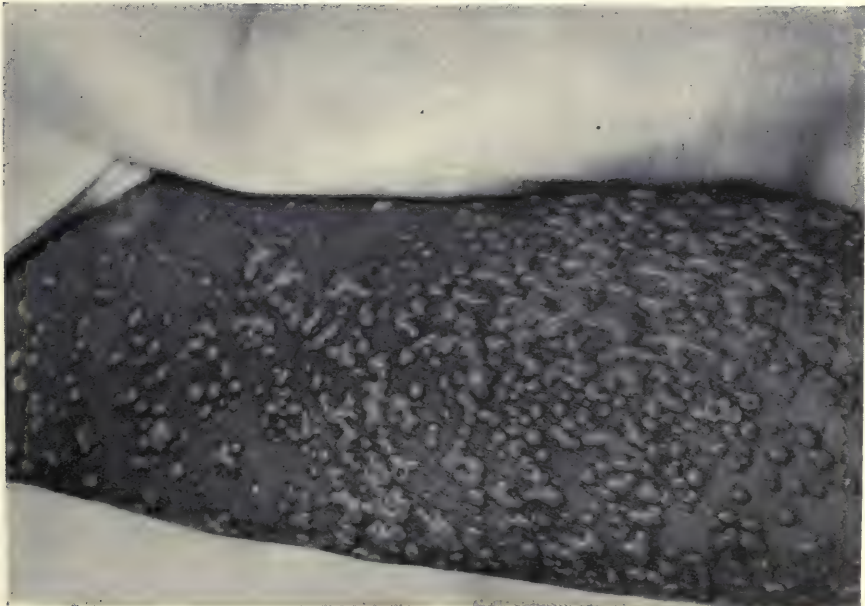
The *pulse*, which has been accelerated in the initial stage, falls with the appearance of the eruption to normal or a little above it. In confluent types it may remain quickened, but seldom exceeds 100, and may be considerably lower. With the secondary fever it again rises, but as a rule is full and regular. In the worst cases very rapid pulses, 120 to 140, are the rule. If the fever is at all prolonged, there is weakness and sometimes irregularity. The *respirations*, except in patients who suffer from laryngeal irritation or pulmonary congestion, are not raised more than would be expected from the level of the temperature. Sometimes the breathing is very shallow and irregular, particularly in fatal cases. The *urine* often contains albumin and, as in the other eruptive fevers, the diazo reaction is sometimes present.

STAGE OF CONVALESCENCE AND DESQUAMATION. In a very large proportion of patients, especially in those who have been vaccinated in infancy, the separation of the crusts does not leave much more behind it than a reddish brown staining which may persist for some months. Scarring or pitting is, however, present in all in whom the true skin has been necrosed during the suppurative process. These scars ultimately become very white and remain visible for life. The separation of the crusts is often a tedious business. On the face particularly new scabs are apt to form as the original ones become detached and it may be ten or twelve weeks before the last one has disappeared. Those in the hair are often a source of trouble. The hair itself falls out in great quantities. The buried crusts or discs in the thick skin of the palms and soles are also troublesome, as they take a long time to work their way through the epidermis, leaving ragged holes in the skin behind them. They can, however, if hard, be easily picked out on the point of a sharp penknife. They are of considerable importance, as the patient cannot be considered as free from infection as long as any remain in the skin. As regards the general condition of the patient himself, the convalescence of small-pox is usually satisfactory and rapid. It is occasionally complicated by small abscesses and glandular swellings, but from the moment the temperature has fallen the patient feels reasonably well and the appetite quickly returns. Emaciation is only well marked in the more severe types of the disease, and when it is present convalescence may be tedious owing to the great weakness of the patient.

COMPLICATIONS. The most important are those affecting the respiratory system. *Laryngitis*, due to the presence of the eruption on the mucous membranes, may be extremely serious. Some degree of hoarseness



A



B

CONFLUENT SMALLPOX.

A—Face of a fatal case (11th day). Pustular stage.

B—Areas of confluence on the thigh of the same patient.

and cough is common in the fever, but, if there is absolute aphonia or any suggestion of dyspnœa, the outlook is very bad. Acute œdema of the glottis occasionally occurs, and in some cases there is ulceration and necrosis of the laryngeal cartilages. *Bronchitis* is often present and may be a source of danger, and occasionally *broncho-pneumonia* supervenes. These respiratory complications are much more frequent in young children than in adults.

The eyes of the patient often suffer severely. Inflammatory processes of all kinds may occur. Severe *conjunctivitis* is relatively common. The cornea may become affected, and ulcers, with resulting opacities, occur. Occasionally there is perforation of the anterior chamber, followed by *panophthalmitis*. I have also seen iritis in a few cases. It is probable that permanent damage can usually be avoided if great attention is paid to the cleanliness of the eyes from the first.

Of other conditions *otitis media* with all its attendant risks is of comparatively common occurrence. *Adenitis* is also a frequent complication, and usually goes on to suppuration. The cervical and axillary glands are those most usually affected. Occasionally the parotid also becomes inflamed. Superficial *abscesses* (see Fig. 21) are often met with, and *boils* are a most common complication in convalescence. As is only natural, when the state of the skin of the patient is considered, the risk of *bed-sores* is greater than in the other acute fevers, even when the greatest care has been taken to avoid their occurrence. *Erysipelas* may occasionally appear during the crusting stage, and I have seen it cause a fatal termination after a patient had been regarded as out of all danger.

There are good grounds for believing that the *orchitis*, which is sometimes present during the acute stage of the secondary fever, should be regarded rather as an exaggerated symptom than an actual complication of the disease. If it were systematically looked for it would be probably found present in a mild form in many of the more severe cases. Only a small proportion of patients suffer from it so severely as to draw attention to its presence. But Chiari, Councilman, and others have found changes in the testicle, peculiar to small-pox, in practically all the testicles they have examined post mortem, and it is suggested that the lesions bear in their extent some relationship to the stages of development of the eruption on the skin. Occasionally small hard nodules may be felt in the testicle during the pustular stage.

Of other complications nephritis is sometimes present, but it may be regarded as a rare condition. Various forms of paralysis are said to sometimes complicate or follow an attack of small-pox. I have not personally had the opportunity of observing any case, but it would appear that in

some instances at least the lesion is a peripheral neuritis. Paraplegia and hemiplegia also may occur.

TYPES OF SMALL-POX. There are curious differences of severity in the **epidemic type** of small-pox. Of late years the seriousness of the disease has appeared to depend on its source. There seem at present to be two main types, the severe European or African variety, supposed to be derived from North Africa, which was responsible for the high case mortality of 16·8 per cent. in London in 1901, and the mild American type, prevalent in the United States, which has been observed in certain small outbreaks in this country and is also believed to have been imported to New South Wales from Vancouver. This latter type is exceedingly benign, and shows a case death rate of from less than 1 to about 4 per cent. Besides this variation in the severity of epidemics we have also to consider similar differences in the manner in which an individual may be attacked.

Mild types. *Varioloid.* While under this heading some writers would apparently include all cases of small-pox which occur in the vaccinated and which are in the least modified, it would appear more reasonable to restrict the term to the very slight and abortive cases which show marked deviations from the normal stages of development of the eruption. The term is perhaps an unfortunate one, as it suggests a condition which is merely 'like small-pox', whereas it is in reality small-pox itself, though in a highly modified form. These mild cases are capable of communicating the most severe types of the disease to other people. They may occur in the unvaccinated as well as in the vaccinated, but no doubt vaccination in infancy, not repeated in after life, has done much to make them relatively common. Being difficult to recognize, they are responsible for much spread of infection, and the symptoms are so mild that the patient is capable of walking about with the disease on him, so that the damage he can do is almost unlimited.

In these mild cases the initial symptoms are often quite severe and the fever high. There may be even initial rashes. The eruption, however, tends to come out rather early than late. Occasionally it may be profuse and show its modification merely by the abortion of a large percentage of its elements. Thus some papules may remain papules, others developing into vesicles, of which again many dry up without becoming pustular. The effect of such an abnormal development is to cause lesions in different stages to be present at the same time on the same area of skin. Sometimes, again, the vesicles may be monolocular, and readily collapse when pricked. A few lesions alone may run through all the usual stages, but these are seldom numerous enough to cause any secondary fever. In other cases the papules may continue to come out as it were in crops for three or four days, instead

of all appearing about the same time. It will be noticed that all these modifications tend to make diagnosis extremely difficult.

In the majority of cases of varioloid the eruption is very scanty, and only a few lesions may be noticed, perhaps two or three on the face and one or two on the wrists. These may or may not develop in the normal manner. In some cases, however, there is no eruption at all, even when the initial fever has been characteristic. Such examples of *variola sine eruptione* have been reported frequently enough to leave no doubt whatever regarding the possibility of their occurrence.

Severe types. The confluent form of the disease has been already discussed. It remains only to consider the hæmorrhagic types. The classification of these is somewhat confusing, and it is often difficult to draw an exact line between the two main types, which are, in fact, merely variations in severity of the same process of profound toxæmia, and, indeed, are included by Ricketts under the common name of 'Toxic Small-pox'. The first type may be called 'True Hæmorrhagic

or Black Small-pox', and is also described as the 'purpuric' form of the disease. In patients suffering from this variety the true eruption does not develop, or is extremely scanty. The initial symptoms are invariably severe, and at first the temperature is high. Erythematous prodromal rashes may be present, as may also those of the petechial variety. If the erythema is general it consists of a uniform flush of a vivid red, gradually turning to a terra-cotta colour. On the second or third day numerous hæmorrhages appear on the skin, especially in the groins and axillæ, but also scattered all over the body, including the face. These hæmorrhagic subcuticular spots vary in colour from a pale purple to black,

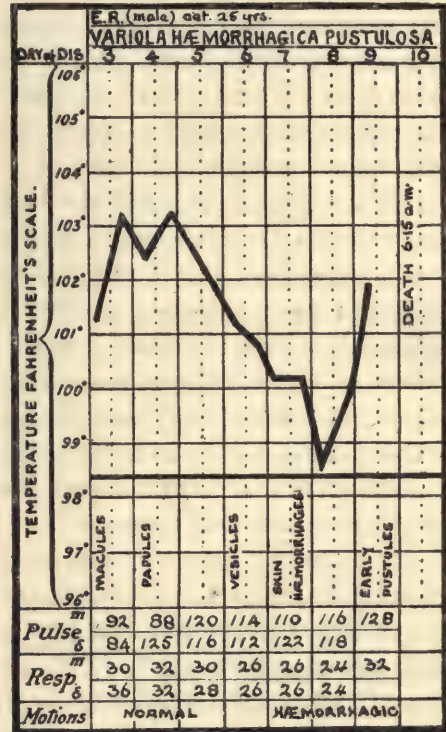


FIG. 25. Hæmorrhagic or toxic small-pox. Note the only partial fall of temperature with commencing eruption. Blood was present in the urine from the fifth day onwards, in the stools from the sixth day. Subconjunctival hæmorrhages and purpuric spots on the skin were observed on the seventh day.

and in the worst cases are extremely numerous. Subconjunctival hæmorrhages occur early, the white of the eye becoming masked, as it were, with blood. The temperature falls slightly with the appearance of the hæmorrhages, and on the third and fourth days may average about 100° , rising only just before death. Bleeding may occur from any part of the body which is capable of hæmorrhage. Epistaxis is common. The urine is scanty and contains large quantities of blood; sometimes indeed it seems to consist almost entirely of blood. In women metrorrhagia is invariable. Blood oozes from the gums, and hæmatemesis and hæmoptysis occasionally occur. The stools often contain blood in large quantities. In addition to the well-defined hæmorrhagic spots on the skin, faint blue bruise-like marks appear in different parts of the body, being, no doubt, often due to light pressure, the patient being in a similar state to one suffering from hæmophilia. The face, if not much involved by the hæmorrhagic eruption, is pale, and the expression anxious. The patient is tortured by extreme thirst. As a rule the mind remains quite clear. The acute consciousness, indeed, of the patients is the most distressing feature of this terrible condition. The pulse is soft and compressible. Death invariably occurs sooner or later, in the worst cases about the third, but more frequently on the fifth or sixth days. By the later date there is usually some attempt of the true small-pox eruption to appear.

In the second type of hæmorrhagic small-pox the eruption of the disease precedes, or immediately follows, the appearance of the hæmorrhages. For this reason it has been called the *Vesicular Hæmorrhagic* form, or '*Variola Hæmorrhagica Pustulosa*', The initial fever may be very severe and prodromal rashes may be present. Hæmorrhages occur, both between the papules and actually into their base. The vesicles develop badly, being flat and empty, and from the hæmorrhage beneath them present a pale violet or blue colour. The pustular stage is rarely reached, except in exceptionally favourable cases. Epistaxis and hæmaturia may occur. The face is swollen and cyanosed, and delirium and mental confusion are the rule. The skin, particularly of the dependent parts, is often deeply stained and of a purple colour. The pulse is rapid and the temperature does not fall to normal in the vesicular stage. Sometimes the hæmorrhages are limited to the base of the vesicles and the surrounding skin is unaffected. Such cases are of more favourable prognosis and occasionally recover, especially if only parts of the eruption are affected by this process. The eruption in these hæmorrhagic cases is usually confluent.

It must be remembered that it is not infrequent in small-pox to see patients in whom hæmorrhage has occurred into the cavity of individual

pocks, the pock becoming filled with blood or blood-stained serum. These can hardly be classed as instances of hæmorrhagic small-pox, as often they present no malignant symptoms and make quite a good recovery. The most dangerous hæmorrhagic eruptions are those in which there are no papules or vesicles present at all, the next most fatal those in which the skin between the vesicles is chiefly the seat of the purpura. Slightly more favourable are those in which the base of the pock is alone involved, while mere bleeding into the cavity of the pock is not of great significance.

SMALL-POX AND PREGNANCY. In the severe forms of small-pox, that is to say, in hæmorrhagic and confluent types, a pregnant woman always aborts if she lives long enough. In some cases the abortion may take place during the initial fever, in others in the pustular or crusting stages. In the discrete and modified forms of the disease abortion is said to only occur in about a third of the cases, and the more advanced the pregnancy is, the more likely is the woman to abort. Even late in pregnancy, however, if the attack is a mild one, abortion may not occur. The last three patients whom I have had under my observation, whose pregnancy was of seven months' duration, were all able to leave hospital without accident. Two of them were discrete, the third merely varioloid. Should abortion occur the outlook for the mother is satisfactory, except of course in the severe types of the fever.

As regards the foetus, it as a rule escapes taking small-pox, but it may be born with the eruption, or may on the other hand develop small-pox shortly after birth, having contracted the disease *in utero*.

SECOND ATTACKS. It is unusual for a person who has had small-pox once to suffer from the disease a second time. But we not infrequently meet with patients who assert they have had the disease before. It is quite possible that in some instances the previous attack has been in reality one of chicken-pox. Out of the three or four alleged cases, however, which I have seen, one, a man of over forty, stated that he had had small-pox in childhood, and the pitting appeared to be absolutely characteristic. The second attack in this case, though a mild varioloid, was also beyond question. The experience of others, much more extensive than my own, goes to prove that such attacks, though exceptional, do occasionally occur, and, from our knowledge of the other exanthemata and other infectious conditions, there is certainly no reason why they should not.

THE BLOOD IN SMALL-POX. The main feature of leucocytosis in small-pox is the marked increase in the mononuclear elements. The polymorph cells seldom exceed 50 per cent. of the whole. Magrath, Brinckerhoff, and Bancroft have made an exhaustive study of this subject, and their results,

briefly summarized, are as follows: During the last days of the incubative period there is said to be a leucocytosis. This is, at the time of onset, changed into a relative or absolute leucopenia. During the formation of the eruption there is a second stage of leucocytosis, followed by a relative leucopenia at the height of pustulation. In the crusting stage the leucocytes again increase in numbers and become more numerous than they have yet been. There is thus a peculiar alternating curve during the illness which is claimed to be characteristic, and which deserves further consideration by other observers.

MORBID ANATOMY AND HISTOLOGY. For information on the histology of the eruption the reader is referred to the admirable work of Councilman¹ on this subject. He summarizes his conclusions as follows: 'The specific lesion of variola is a focal degeneration of stratified epithelium, vacuolar in character, and accompanied by serous exudation, and the formation of a reticulum; the fully developed product of these processes being a characteristic multilocular pock or pustule. The occurrence of these lesions is sharply limited to the stratified epithelium of the skin, and of the mucous membranes of the soft palate, the pharynx and œsophagus. The typical lesion begins with degeneration of the cells of the lower layers of the epidermis, accompanied by exudation, at first serous, later more or less cellular, the products of which are contained within a reticulum formed by the degenerated cells. The lesion becomes a well-filled pustule by increase in the amount of the exudate and rupture of the fibres of the reticulum. This development may take place wholly within the epidermis, or the corium may become involved and form the bottom of the pustule. The lesion subsides by the removal of the fluid portion of the exudate by absorption and drying, and by the degeneration of the epidermis, in the course of which the residual mass of degenerated epithelial cells, leucocytes, and débris, enclosed between two layers of horny epidermis, the old and the newly formed, is exfoliated. The lesions in the mucous membrane start in the same way; but in the absence of a horny layer the degenerated cells are cast off, and the vesicle is rarely seen and the pustule never.'

As regards other lesions which may or may not be specific, Councilman draws attention to the great proliferation of cells in the hæmopoietic organs. Large numbers of mononuclear basophilic cells are formed and give almost a specific character to the blood. Infiltration with these cells, focal and interstitial in distribution, occurs constantly in the testicle, and by pressure and thrombosis causes anæmic focal necrosis, lesions which may be classed as specific. The paucity of polynuclear cells, alike in the specific lesions,

¹ Councilman, *Journal of Medical Research*, February, 1904.

in the focal degenerations, and in the bone marrow, is a condition so constant and so pronounced as to render it a striking peculiarity of the disease.

Of the changes found post mortem in the various organs it is sufficient to say that for the most part they resemble those presented by cases of the other acute toxic conditions. The lesions caused by the eruption on the mucous membranes may be seen in the œsophagus, larynx, and trachea. The lungs usually present marked hypostatic congestion, and the bronchial tubes are often filled with muco-pus. The heart muscle is degenerated. The spleen is enlarged, soft, and occasionally diffuent. The liver and some of the other organs may present small focal degenerations. The most characteristic site of these, however, is the testicle, in the interstitial substance of which are found dense yellowish foci varying in size from that of the head of a pin to that of a pea. Small foci of necrosis and hæmorrhage have also been observed in the bone marrow, the most striking change in which, however, is said to be the extraordinary reduction in numbers of the polynuclear leucocytes. Pocks may be sometimes observed in the rectum and vagina, but are never found on the serous membranes. In hæmorrhagic cases numerous hæmorrhages are to be seen in the muscles and most of the viscera.

DIAGNOSIS. The diagnosis of small-pox falls naturally, as it were, under two headings. We may have difficulties in recognizing the initial fever, and secondly we have to distinguish the eruption from others which may resemble it.

The diagnosis of the initial fever may be a matter of extreme difficulty, unless indeed there is definite evidence of the exposure of the patient to infection. Its most marked features, as we have already seen, are high fever and marked prostration, accompanied by headache, shivering, pain in the back, and vomiting. These symptoms in themselves do not help us much to distinguish the onset of small-pox from any other acute condition, and if there is no outbreak of the disease in the locality at the time, it is extremely unlikely that a diagnosis will be made until the eruption appears. The exception to this, however, is that if a petechial rash is present, and if that rash is typical in its character and in its distribution on the lower part of the abdomen, the case is undoubtedly one of small-pox. If, on the other hand, we are on the look-out for small-pox, the mere presence of the group of symptoms detailed above should make us extremely suspicious that the case is one of that disease, and if, further, the patient has been definitely exposed to infection between one and three weeks previously, he must be isolated at once. But it must be remembered that in small-pox all these initial symptoms are not invariably present.

Pain in the back, which is so much spoken of, only occurred, for instance, in little more than half my cases, and in many of these it was not so marked as to cause the patient voluntarily to complain of it. When, however, it is present, it is certainly highly suggestive.

The most difficult disease to distinguish from small-pox during the initial stage is, in my opinion, unquestionably *influenza*. All the symptoms mentioned above may be present, the backache in particular being very prominent. When both fevers are epidemic, as sometimes occurs, it is, I think, practically impossible to come to a diagnosis unless, of course, a definite petechial rash is present. A pulse, relatively slow, when considered along with the temperature, would be a strong point in favour of influenza, but in very severe forms of that infection the pulse is occasionally quite rapid at the onset. In the vast majority of cases it will be necessary to wait till the small-pox papules commence to appear before we can come to a definite decision. If nothing is seen by the fourth day it should be fairly safe to conclude in favour of influenza.

It is said that *lumbago* has been sometimes mistaken for small-pox. No doubt severe pain in the back suddenly attacking a person who has been exposed to infection is a disquieting symptom, but the absence of any fever or headache, both always present in small-pox, should clear up the case.

Further differential diagnosis in the initial stage is limited to the distinction of the various erythematous rashes, met with at this period, from the exanthemata and other forms of erythema. Perhaps the most important disease to consider is *scarlatina*, which from the abruptness of its onset, its headache, vomiting, and chills, bears a considerable resemblance to small-pox with a scarlatiniform prodromal rash. In making the distinction much depends on the examination of the throat. In scarlatina this is always more or less injected, even if sore throat, a rare complaint in small-pox, has not been actually complained of. The soft palate, moreover, in scarlatina is usually definitely congested and presents a punctate rash; in small-pox we may have the good fortune to see early lesions of the eruption in this situation. In both diseases the tongue is heavily coated, but there is no definite enlargement of the papillæ in small-pox. The facies of the patient may be of some assistance. The circumoral pallor of scarlatina is lacking in the small-pox patient, whose face is generally uniformly flushed. If we examine the rash itself we may observe slight differences. That seen in cases of small-pox is more diffuse and does not show distinct punctation. It is a more or less uniform flush. It is, too, more likely to be irregularly distributed than the rash of scarlatina, and may be only partial and not general, even on the trunk, a state of affairs not usual in the milder infection.

The most difficult cases are those in which an intense scarlatiniform rash is the precursor of an attack of hæmorrhagic small-pox. Small petechial spots are not infrequently met with in the groins and on the upper part of the chest in sharp cases of scarlatina, and, when combined with a vivid rash, give an idea of a stained punctation which may be most confusing. I speak feelingly on this point, as I remember seeing a case which I was convinced was one of scarlatina till the multiplication of definite purpuric spots on the skin put the issue out of doubt. As regards the symptoms complained of by the patient, backache is almost unknown in scarlatina, and, if small-pox is epidemic, should arouse suspicion. On the other hand, sore throat should turn our thoughts to the less dreaded fever. It is reassuring to know that children of under ten years of age, suffering from small-pox, do not have scarlatiniform initial rashes.

Morbilliform varieties of erythema are liable to be mistaken for *measles*. As has been said above, the appearances of the eruption of true measles may be most closely imitated. The macules, however, are not raised above the skin level, and the rash, on fading, leaves no staining behind it. The colour is also somewhat paler than that usually seen in measles. Still the presence of such a rash, in a person suffering from high fever, must always cause some difficulty in diagnosis. The absence of catarrhal symptoms and of any history of coryza or coughing for some days previous to the appearance of the rash, would be points much against measles. The examination of the buccal mucous membranes is important. In measles, even in the eruptive period, there is characteristic congestion and stomatitis. Koplik's spots should also be visible on the first day of the rash. Small-pox, in this initial stage, presents no appearances of the mucous membranes likely to be confused with these conditions. It may be noted also that vomiting, backache, and marked shivering are symptoms most unlikely to occur in measles, and the very sudden onset of small-pox and the early prostration of the patient may be contrasted with the more insidious commencement of the other fever. As will be seen below, this question of the differential diagnosis of small-pox from measles may arise again when the small-pox papules make their first appearance.

Other rashes may possibly, in rare cases, be confused with the prodromal rashes of small-pox. It is unlikely, however, that much difficulty will be caused by them, except in persons who are known to have been exposed to small-pox infection. *Erythemas*, due to shell-fish and to irregularities of diet, may be accompanied with severe vomiting and sometimes prostration, the symptoms appearing quite suddenly. But in such cases there is no fever, which is quite enough to put small-pox out of court. Multiform

erythema, on the other hand, may be accompanied with a considerable rise of temperature. In such a case the history of similar previous attacks, or of any pre-existing rheumatic condition, would make us hesitate to call the case small-pox, and it would be safer to isolate at home and wait for the true eruption before notifying the patient as such. Syphilitic roseola, copaiba rashes, and rubella are associated with too little pyrexia and too trifling constitutional symptoms to cause serious trouble.

Diagnosis in the stage of eruption. In the papular stage the most probable mistake is to confuse the eruption with that of *measles*. The two eruptions are often first visible in the same situations, the face and forearms. In coming to a diagnosis, stress must be laid on the history of the case, whether the eruption has been preceded by catarrh or by initial symptoms more suggestive of small-pox. The mouth must receive attention. In a patient whom I recently saw, and who had been notified as small-pox, it was the presence of definite Koplik's spots in the mouth which determined the diagnosis, otherwise extremely difficult, as there had been a possibility of exposure to both diseases. It must be recollected that measles papules may be exceedingly hard and, on the brow, may be quite shotty to the touch, whereas in small-pox, especially if modified, the skin lesions may be almost soft. If in doubt, it is wise at the first inspection of the patient to take the temperature, and make another visit four or five hours later. If it is falling, with the eruption still increasing, it is almost certain to be small-pox; if rising, the probabilities are in favour of measles. Again, in small-pox, attempts at early vesiculation may be sometimes seen in the papules. Any suggestion of this in measles requires a lens to make it visible. Lastly, when a papular rash is visible on the face in small-pox, it is usual to find definite vesicular lesions on the palate, which are not likely to be mistaken for the mottling seen in measles in that situation. It is, of course, in this distinction, as in that from all other diseases, always desirable to look in the groin for traces of a petechial prodromal rash. If one is found to be present, the diagnosis of an otherwise difficult case is rendered quite simple. It must also be remembered that the measles eruption covers the whole body and does not spare those parts, the flank for example, which usually escape lightly in small-pox. In the vesicular stage our chief difficulty lies in the differentiation of the disease from *varicella*. While the distinction between the two eruptions is sufficiently broad, the diagnosis may occasionally be very delicate, especially when we are dealing with examples of varioloid. In that highly modified condition many of the main rules for distinguishing the diseases fail us. It will be advisable, however, to give them in the first place and to discuss their limitations afterwards.

In the first place, then, to consider the *initial symptoms* of the patient. As a rule, in chicken-pox the eruption is the first symptom. In small-pox, as we have seen, there are always prodromal symptoms, usually of considerable severity. Occasionally high fever occurs in chicken-pox, but this is usually not to be expected till the eruption has fully developed. Sometimes comparatively severe symptoms usher in an attack of chicken-pox, vomiting, shivering, and even convulsions, but, except in rare instances chiefly observed in adults, the eruption may be expected to appear with them, or immediately after them.

Secondly, the *distribution* of the eruption and the sites of its first appearance are of great importance. In chicken-pox the first spots are nearly always observed on the trunk, the face not being affected till several hours, often twenty-four, later. The reverse is the case in small-pox, the eruption appearing first on the face and wrists. When the exanthem is at its height it will be observed that in chicken-pox the trunk, and more especially the back, suffers most. The face is involved to a lesser degree, the upper arms and thighs still less. The forearms, hands, and feet suffer least of all; indeed, I have seen dozens of cases of chicken-pox which did not present a single lesion below the elbow. The comparative immunity of the forearm and hand, in fact, is to my mind one of the most important distinctions of chicken-pox from small-pox. It will be remembered that in small-pox the greatest number of lesions are invariably found on the face, forearms, and wrists; that the legs, upper arms, and thighs are also well covered, if the eruption is at all profuse; and that the trunk and especially the abdomen are usually least affected. The presence of many lesions in the palms and soles would form a strong argument against chicken-pox. On the other hand, the presence of many lesions on the flanks, if the eruption is otherwise scanty, favours a diagnosis of that disease.

Thirdly, as regards the *appearances presented by the eruption* and its manner of development, there are important distinctions. In varicella the papular stage is often missed altogether, the lesion appearing first as a vesicle. In any case the development is much more rapid than in small-pox. When the vesicle has appeared, the superficial character of the chicken-pox lesion allows it to assume irregularities of shape which are seldom or never met with in small-pox. The most characteristic shape is oval, and the thin-walled vesicle, containing very clear fluid at the moment of its first development, and apparently lying *on* rather than *in* the skin, bears little or no resemblance to the more deeply set, conical, or rounded small-pox lesion, with its opalescent contents. Usually, even in difficult cases, some of these oval vesicles will be visible, especially on those parts of the body where, as in the axilla or groin, a fold of the skin seems to assist in exaggerating their length. To the

touch the characteristic chicken-pox vesicle is soft and even velvety. It must be remembered, however, that, on the arms and legs particularly, the vesicles may be small, hard, and almost shotty, and much more deeply set in the skin than they are on the trunk. If pricked, the chicken-pox vesicle collapses readily, it being unilocular. We have seen that the vesicle of small-pox retains its shape owing to its being multilocular. Umbilication, properly so called, is not met with in chicken-pox. Occasionally the partial evacuation of the contents of a vesicle, owing to accidental rupture, leads to a condition resembling it. The small orifice through which the fluid has escaped scabs over. If it is in the centre of the pock, any increase in the amount of the remaining fluid, now usually purulent, causes the periphery of the vesicle to swell up round a central depression, and a condition of 'false umbilication' results. In cases, otherwise difficult to diagnose, this adds much to the confusion if the lesion is not very carefully examined. Such a vesicle often shows considerable puckering round its edges, a point of some importance in diagnosis.

The eruption of chicken-pox has further this distinction from that of small-pox, that, unlike it, it does not come out all at once, but appears in successive crops, each of which takes its own time to pass through the various stages from papule or vesicle to crust. As a result the patient may present, at the same moment on any given area of skin, lesions in all stages, vesicles, pustules, crusts, lying side by side. In small-pox, while the face and fore-arms may present lesions slightly in advance of those on the thighs and legs, a given area of skin in any part of the body may be trusted to present lesions practically identical in their stage of development. This rule, however, useful as it is in making a broad distinction between the two diseases, has marked limitations. As regards the crusts, those of varicella are extremely superficial and not deeply set or buried in the skin.

Fourthly, in making this differential diagnosis we are influenced to some extent by the age of the patient and the condition regarding vaccination. In a child of under ten years of age, in countries where vaccination in infancy is the rule, the presumption is all in favour of varicella. If the vaccination marks are good this presumption is increased, and becomes stronger the younger the age of the child. In older persons, on the other hand, even with poor vaccination marks, there is no reason why the disease should not still be varicella. It is well to remember that the main reason that we do not see more adults suffering from it is because it is so commonly contracted in childhood. Some persons bear characteristic chicken-pox scars. If these are noticed in a doubtful case the diagnosis of small-pox is made, as second attacks of chicken pox need not be seriously considered.

PLATE XIII.



SMALLPOX.

The eruption on the ankle, pustular stage. Note the grouping of the lesions over the malleolus.

The above, then, are the rules on which we naturally lay most stress. What are the exceptions? Unfortunately they are numerous; otherwise the question would present few difficulties. There is no doubt whatever that some chicken-pox patients, usually adults, suffer from a distinct initial fever, sometimes moderately severe, and accompanied by malaise, chills, and even initial rashes of an erythematous type. This fever may last as long as two days. Next, as regards the distribution, we occasionally meet with cases of chicken-pox in which the forearms present quite a respectable amount of eruption (see Plate XVII). The pocks, too, in this situation tend to resemble those of small-pox, in that they are often deeply set in the skin and distinctly shotty. Again, in varioloid, we may meet with almost any peculiarity. I have frequently found, for instance, monocular lesions which emptied completely on pricking. Of the diagnosis of some of these cases, at least, there could be no doubt, as there were members of the same family suffering from unmodified small-pox at the same time. In varioloid, also, the irregularity of the development of the eruption and the frequency of the abortion of some of its elements lead to appearances on the skin which may resemble varicella. Thus, on a given area of skin we may meet with papules which are slowly receding without becoming vesicular, vesicles which are drying up without becoming pustular, pustules unbroken, and pustules ruptured and crusting. It has already been noted that umbilication may be imitated in a chicken-pox eruption.

In coming to a conclusion, then, we must weigh the evidence carefully. In the first place, it is necessary to thoroughly grasp the fact that a severe case of chicken-pox with a profuse eruption presents a very much more formidable appearance than many cases of small-pox (some eruptions are extraordinarily profuse, and cases have been reported with as many as 360 spots on the face). Secondly, we must not be too ready to be misled by the history. The strongest point in favour of a diagnosis of small-pox would be a definite prodromal fever with really well-marked backache. Otherwise it is safer, particularly in adults, to discount much of the value of initial symptoms in coming to a conclusion. I am accustomed myself to lay most weight on the distribution of the eruption and the state of the patient regarding vaccination and revaccination. It is absolutely necessary to examine thoroughly every part of the patient's body, and it is a good plan, with children at all events, to strip him absolutely naked and thoroughly appreciate the distribution of the eruption by seeing all the body at once. When this cannot be done, each part must be examined systematically in turn. A careful search must be made for the large oval vesicles which, if seen, are so characteristic of varicella. A very important point is the facies

of the patient. In small-pox the look expresses prostration or apathy, if the eruption is at all profuse. A patient, then, with a copious eruption and a bright and alert expression will usually, if there is any real doubt in the diagnosis, turn out to be suffering from chicken-pox.

Small-pox has also to be distinguished from various pustular eruptions. Of these *acne* may occasionally be a source of some difficulty, though if a small-pox eruption has developed at all normally the diagnosis should be simple enough. To distinguish, however, cases of *acne* from mild examples of varioloid is not always easy. Three main points should be considered, the presence or absence of general constitutional symptoms, the distribution of the spots, and their character as regards vesiculation. A history of initial symptoms, a general distribution with special localization on the face and forearms, and definitely vesicular lesions would all point strongly to a case being small-pox. In *acne* there are no prodromal symptoms, the eruption though pustular, is not accompanied by pyrexia, the distribution is chiefly on the face and shoulders, and there is no vesicular stage in the development of the spots. Further, though a few scattered lesions may be of large size, and individually may present some resemblance to the small-pox pustule, many are acuminate, and in most there is a central dot or comedo. The presence of these 'blackheads' in other parts of the face and the history of previous similar eruptions will often clear up the case.

As regards *drug eruptions*, such as those caused by the bromides and iodides, the absence of constitutional symptoms, and the irregular development of the eruption considered together with the fact that the drugs have been taken, should prevent much difficulty. These eruptions, however, have a very similar distribution to that of small-pox, and also present a distinct vesicular stage. Often the appearance of the large bullæ, which not infrequently occur, eliminate the possibility of the case being one of small-pox.

Herpes has been mistaken for small-pox, but its grouping and distribution are entirely different. The vesicles are usually confined to one small area on which they are set closely together. When on the palate they resemble those of small-pox in appearance, but there are no initial symptoms and the distinction between the two conditions should not be difficult. Small-pox has also been occasionally confused with a *pustular syphilide*. Here we may have some fever and constitutional symptoms, but the frequent presence of scaly copper-coloured papules, together with the pustules, and the invariable enlargement and induration of the inguinal glands in syphilis should assist in making the diagnosis. *Glanders* may also have to be considered. In a case which I recently had under my care the pustular eruption on the chest and face bore a certain superficial resemblance to small-pox. The

wrists and forearms, and indeed the rest of the body, were, however, quite free from any eruption, and the large granulating buds on the brow and scalp caused an appearance quite unlike that seen in small-pox. The presence of fetid nasal discharge is a very strong point in favour of glanders, but in some cases, as in the one just mentioned, the nose remains quite dry.

It is interesting to note that in the opinion of Ricketts, whose exceptionally large experience of small-pox renders him a particularly reliable guide, the distribution of the eruption is really the main point to be considered in diagnosis. All interested in the subject should read his monograph for themselves. It is sufficient to say here that, when we consider the fact that most of the small-pox seen in this country is modified by vaccination in infancy, the appearance of the individual lesions themselves is not likely to afford us information as accurate as that supplied by the distribution, which appears to follow the same laws both in modified and unmodified small-pox. And this distribution, affecting, as it does, those parts of the body which are irritated by exposure, by the friction of clothes during various movements, and so forth, will serve to distinguish the fever not only from such diseases as varicella or measles, but also from drug eruptions and pustular skin conditions. To take an example: Ricketts refers to the armpit as 'a mine of information'. In that protected part of the body there is an almost invariable immunity from the small-pox eruption. In other conditions, however, lesions often occur in that situation. In a large number of cases of varicella which I have recently observed, spots were present in the axilla, even though the eruption was relatively scanty. To take yet another point: the gradation of the density of the eruption from the upper arm to the forearm, the latter suffering most, is a characteristic feature of small-pox, most unlikely to be observed in the conditions liable to be mistaken for it.

Vaccination may be used as a final test in diagnosis. Of seventy-five cases reported by Hanna, forty-six, vaccinated between the day of infection and the day of onset, showed the concurrent lesions of small-pox and vaccinia, as did also two out of three vaccinated on the day of onset. The remaining twenty-six patients, vaccinated between the second day of illness and the fourth day of eruption inclusive, did not develop vaccine vesicles. The tendency of small-pox lesions to develop profusely round a recent scratch accounts, in Hanna's opinion, for successful results which have been reported later. We may conclude, then, that if typical vaccine vesicles develop in a case, vaccinated after the suspected eruption has appeared, the disease is not small-pox.

PROGNOSIS. In estimating the chances of recovery of a person who has been so unfortunate as to contract small-pox, we are in the first place influenced by his condition as to *vaccination*. Has he been vaccinated at all? Has his vaccination been only in infancy, or has he by any chance been revaccinated? If vaccinated, what is the condition of his vaccination marks as regards, firstly, number, secondly, superficial extent, and thirdly, foveation? By the latter we understand the slightly pitted and honey-combed appearance of the really good scar. As will be seen later in the chapter on *vaccinia*, all these points are of importance in estimating the degree of protection which the patient is likely to possess. Even if the vaccination has been insufficient to protect against infection, it may be most efficacious in modifying the severity of the attack. A revaccinated person seldom contracts small-pox, and if he does so, always provided he shows good marks, it is most unlikely that the disease will run a severe course. The length of time which has elapsed since vaccination, or revaccination, is also a potent factor in determining the prognosis.

Age, then, is of much importance when we have to deal with persons who have been vaccinated in infancy and not afterwards. The younger the patient, the more certain is his recovery. Under ten years of age few vaccinated subjects die. As age increases so also does the mortality, reaching perhaps 12 to 16 per cent. in patients of over thirty years of age, according to the severity of the epidemic. In the unvaccinated, on the other hand, the first five years of life are the most fatal, the death-rate in those years probably exceeding 40 per cent. The second quinquennium gives a considerably lower mortality rate, probably less than half of the above, as do also the years between ten and twenty. Thereafter the mortality rises steadily with increasing age, and in persons of over forty years of age may even exceed that of young children. The marked difference of fatality between vaccinated and unvaccinated children of under ten years of age will always remain one of the most remarkable evidences of the value of vaccination.

As regards *sex* it is possible that females have a very slightly worse chance of recovery than males. The difference, however, is so small as to be hardly worth consideration.

It is well to remember that much depends upon *epidemic type*. Small-pox can be most astonishingly trivial. The recent extensive outbreak in Sydney is a case in point. Although affecting a population for the most part unprotected by vaccination, it was very mild in type and practically without fatality. Similar benign epidemics have been described as occurring in the States.

And now, leaving these general considerations and coming to the indi-

vidual patient, we must consider what are the features of any attack of the disease which may be regarded as favourable or unfavourable to the patient. All agree that a mild *initial fever* means a mild case. The converse, however, is not true, as very severe initial symptoms occasionally precede the mildest of varioloids. As far as *rashes* are concerned, the morbilliform variety is usually considered a more favourable prognostic sign than is the scarlatiniform, that is to say, this form of erythema is less likely to be associated with a severe type. The very vivid lobster rash is, as we have seen, as a rule, the precursor of a hæmorrhagic attack, and is therefore of most evil omen. The appearance of distinct hæmorrhages with an irregularly distributed scarlatinal erythema is also to be regarded as a fatal sign. My experience of petechial groin rashes is that, while they are occasionally, though infrequently, met with in varioloid, they occur most frequently in the confluent forms of small-pox, and are fairly common in the discrete variety. With marked exceptions, then, we may conclude that a patient who presents such a rash is more likely to have a severe attack than not.

Very intense pain in the back, as an initial symptom, should be, as a rule, regarded as a bad sign. Hæmorrhagic cases often present this symptom in an exaggerated form.

When the true eruption has made its appearance, a rapid fall of *temperature* to normal should always be looked upon as a most favourable sign. The completeness of the remission and the maintenance of the temperature at the normal level for some days may be taken to indicate that the secondary fever will not be very severe. Conversely, if the fever merely abates, without the normal being attained, a severe attack may be expected. The amount of the *eruption* itself usually bears a direct relation to the severity of the case. It is true that certain examples of varioloid may present an extremely profuse eruption, but in this form of the disease it is usual to notice abortion of many of the lesions almost from the first. Such an early drying up of some of the vesicles is always a good sign. Apart from these cases, however, the greater the number of the pocks the more risk is to be expected when the secondary fever commences, as the dangers of the latter depend more or less directly on the amount of suppurating material in the skin. A rapid development of the lesions, each stage being comparatively short, may be held to be a sign greatly in favour of the patient's recovery. In unmodified small-pox the development is slow, and we may in some degree judge the amount of protection preserved by the vaccinated by the slowness or rapidity with which their lesions develop. If, then, the vesicle becomes rapidly milky and opaque, we may conclude that the attack will be more or less modified.

The dangers of the *secondary fever* are in proportion to the number of

suppurating pocks and the height and duration of the pyrexia. A case with a high temperature, over 103° , a rapid pulse, exceeding 120, and with marked delirium and nervous symptoms, will always cause anxiety and great caution in prognosis. Any suggestion of sudden hyperpyrexia is a bad sign. It too often precedes death. Rapid respiration, suggesting hypostatic congestion or a broncho-pneumonia, is also a reason for alarm. Edema glottidis, or indeed any marked laryngeal symptom, is of course most dangerous. In severe cases the eleventh, twelfth, and thirteenth days are always anxious. Sometimes, however, a patient may survive this critical period only to die from exhaustion or from some intercurrent complication afterwards. Abortion in confluent cases leaves little hope for the mother.

The mortality of *confluent* cases of unmodified small-pox is probably, taken all over, not less than 60 per cent. Children of under two years of age cannot be expected to recover. Confluent small-pox in the vaccinated, although very serious, is hardly so fatal. Cases, on the other hand, in which the eruption remains discrete usually recover, and it is rare for a vaccinated person with this variety of the disease to succumb, unless indeed some intercurrent complication is present.

Hæmorrhagic cases may be regarded as invariably fatal. The first appearance, then, of hæmorrhage on the skin, or from the kidneys or bowels, is the worst of all signs. Hæmorrhage, however, into the pocks themselves, or into their bases, particularly if this symptom is limited to the lower extremities, need not cause too much alarm. The really dangerous sign is blood extravasation into the skin between the pocks.

TREATMENT. The indications are, firstly, to maintain the strength of the patient by suitable diet and medication, and, secondly, to treat the local skin condition with a view of so far as possible modifying its development, and preventing subsequent disfigurement. We may first consider the general management and treatment of the disease, and thereafter the local treatment.

General treatment. The patient should be placed in airy surroundings, and if possible there should be an allowance of at least 2,000 cubic feet per bed in small-pox hospitals. Too much light is, I think, a disadvantage. In any case direct sunlight should not be allowed to play upon the face of the patient. During the initial fever the diet should be fluid, and is best limited to milk. At this stage, as might be expected, the patient has no appetite. Headache is perhaps best treated by icebags to the head. Such drugs as phenacetin or caffeine may also be tried in moderate doses, but they are often disappointing. When the pain in the back is very severe, hot applications occasionally give relief. Insomnia at this stage may be treated with a com-

bination of bromide and chloral, with bromidia, or with such drugs as sulphonal or veronal. If the fever is very high, cold sponges may be used frequently. In any case the patient should be sponged twice a day with tepid water.

With the appearance of the eruption and the accompanying fall of temperature the appetite usually returns. Discrete cases are perfectly capable of dealing with a normal diet during the vesicular stage, unless, indeed, the eruption is particularly copious in the mouth, when naturally solids are taken with difficulty. A liberal diet of soft solids is, I think, most suitable for patients of all types at this stage, provided the temperature is not much above the normal line. To maintain too rigid a dietary is to leave the patient weakened, just at a time when he is likely to require all his strength. Eggs, milk puddings, white fish, vegetable soups, and even minced meat in moderation, may be given at this period.

Hoarseness and laryngeal irritation, as well as the sore throat often caused by the development of pocks upon the fauces during this stage and later, are best treated by frequent inhalations of steam, a few drops of creasote or benzoin being added to the water in the inhaler. Insomnia at this period is usually due to skin irritation, and I have found opium more efficacious than any other drug for its relief. A 5-grain Dover's powder is my favourite prescription, and will usually secure sleep. If not, it can be safely repeated two or three hours later, and in that case seldom fails.

During the secondary fever the diet must again be fluid. Milk should be given in measured quantities at measured intervals, and, if there is any tendency to vomiting or sickness, may with advantage be diluted or peptonized. Such foods as Benger's, plasmon, or sanatogen may also be used. Beef and chicken tea, egg-flip, and fruit jellies may be given to reinforce this dietary. If the pulse exceeds 120 in an adult stimulation will often be necessary. Whisky or brandy is probably the most convenient and suitable form in which to give alcohol. In very prostrate cases it is well also to try champagne. I have not seen much good result from cardiac tonics, although I occasionally use strophanthus. In patients whose breathing is laboured owing to hypostatic congestion, strychnine is frequently most useful. Should the temperature tend to rise to hyperpyretic levels, ice to the head and ice-cold sponges may be tried, but it is unlikely that any permanent good will result. Cold applications are also useful if there is marked delirium, sometimes having a distinctly soothing effect. During this stage delirium is occasionally of a very excited and violent type, and to control the patient hypodermic injections of the hyoscin and morphia compound may be required. If the circumstances allow, and there is time for the drug to act, a

dose of sulphonal, 25 grains, given early in the evening and followed up, if sleep is not secured within four hours, by drachm doses of paraldehyde repeated every half-hour, may be efficacious, but too often the excitement comes on so suddenly that an injection must be given. While waiting for drugs to take effect, a tactful nurse can do much to keep the patient quiet. It is probably better to let him leave his bed and walk about the ward, if the fancy takes him, than to irritate him by holding him down, as struggling will only exhaust him the more.

In very severe cases a water-bed is occasionally of advantage. Every movement of the patient increases his discomfort, and, however comfortable an ordinary bed may be, it is difficult for him to rest quietly owing to the irritation and actual pain caused by the pocks on his back and limbs. The weight of the bedclothes is often complained of, and, when this is the case, a cradle may be employed to carry them. If the smell of the crusting eruption is particularly offensive either to the patient himself or to others in neighbouring beds, *sánitas* or some similar disinfectant may be frequently sprinkled on the floor round his bed, or creasote may be vaporized at the bedside in a metal basin with a spirit lamp beneath it. Free ventilation is, of course, at all times an essential.

The toilet of the *mouth* and of the *eyes* is of the greatest importance both for the comfort of the patient and the preservation of his sight. The mouth should be cleaned out every four hours if necessary, and swabbed with an ointment of boracic acid and vaseline to which some peppermint oil has been added, or else boroglyceride may be employed. If gargling is possible it should be encouraged, a gargle of boroglyceride or listerine in warm water, or of peroxide of hydrogen, being suitable for this purpose. It has been suggested, and seems very reasonable, that in cases where deglutition is very painful, the throat may with advantage be sprayed with cocaine before each feed. Occasionally rectal feeding may be necessary. A laryngeal case may in this stage require a steam tent, and, should obstruction become marked, the question of tracheotomy must be seriously considered. As regards the eyes, they should be bathed frequently with boracic lotion or weak corrosive solution. The lids should be smeared with vaseline and every care taken to prevent them becoming glued together. If the cornea becomes affected, an ointment containing yellow oxide of mercury and atropine is probably the best preparation.

Discrete cases, in which there is little or no secondary fever, may be given a normal diet, if the state of the mouth permits, and require nothing in the way of treatment except locally. In *hæmorrhagic* cases, on the other hand, treatment, however active, is of little or no avail. I have seen no benefit

follow the administration of hæmostatic drugs, such as hazeline, ergotine, and the like, which are all equally ineffective. Nevertheless, they should be employed, as also should stimulants, if called for, however hopeless the case may be. The direct injection of normal saline solution into a vein may also be tried, though here again we may regard the treatment as less likely to benefit the patient than to satisfy the conscience of the medical attendant, who naturally and rightly prefers, even against all experience, not to give up a case as hopeless, but to leave no stone unturned in his efforts to save a life.

Local treatment and attempts to abort the eruption. For the average patient it is rather the local than the general treatment which is of importance. Even in mild cases the development of the eruption is uncomfortable and often painful, and in those which are more severe, the fever, delirium, and other general symptoms are due entirely to the septicæmia which it causes, and the intense skin irritation which accompanies it. Again, any local applications which are likely to limit the extent of the necrosis, and so diminish the chances of the skin being left badly 'pitted', are obviously of advantage. Many ointments have been suggested for this purpose, and some may be of service, but latterly the tendency has been to use the most simple methods for the comfort of the patient. Of these a light mask of lint frequently soaked in iced water and kept thoroughly moist is probably as useful as any, similar fomentations covered with gutta-percha tissue being applied to the hands and arms, and other parts chiefly affected by the eruption. Some patients, however, will not tolerate even a mask, and for them I usually use carbolized vaseline lightly smeared over the face. When the pocks have commenced to rupture and the odour has become offensive, a little iodoform may be added to the vaseline. Later, if the separation of crusts has left raw surfaces, zinc ointment may be useful. Another application to the face which has been well spoken of is peroxide of hydrogen, compresses being soaked in it and frequently renewed.

Tincture of iodine, painted daily on the face from the early stages of the eruption, is said to be beneficial. I have had no experience of it, but it seems worth trying. During the stage of desiccation, when the itching is often very distressing to the patient, a lotion consisting of one part of dilute acetic acid to three of water may be recommended. The frequent use of *warm baths*, however, is more likely than anything else to give comfort to the patient at this time. The warm bath, indeed, should be used from the earliest possible moment after the pocks have commenced to rupture. Discrete cases, with little or no secondary fever, may of course be allowed baths throughout, and will very much appreciate them. In the confluent

cases, however, we must be guided by the general condition of the patient, when determining whether the bath is advisable. If prostration is extreme it is better to defer its use. The continuous tepid bath has been strongly recommended, and, were it not for the difficulties of carrying out this treatment, and the extra nursing which it entails, it would seem a most rational method of dealing with the secondary fever, and one which would assuredly be very grateful to the patient. Should it be used, some mild antiseptic, such as boracic acid, should be added to the water, which requires frequent changing. There is no reason why a patient should not remain for many days in such a bath. The practical difficulties, however, of applying this method, especially in a temporary building not too well equipped with the conveniences for it, have always prevented me making use of it. Ordinary warm baths, on the other hand, can always be given, and, if necessary, they may be repeated several times in the day and made as prolonged as possible. The crusts loosen more quickly and any purulent matter is quickly washed away, which is certainly to the advantage of the patient.

To aid the process of desquamation of the crusts McCombie advises the use of ordinary linseed *poultices* sprinkled with iodoform. These can be applied to the scalp in the ordinary manner, and for the face the poultice can be spread thinly on a lint mask. I have in the later stages of desiccation used starch poultices in this manner to detach the crusts, and have found them of some advantage. As apart from the definite crusts themselves, sticky material often adheres to the skin of the face in places, particularly round the nose. How far this is actually infectious if it returns, after being once removed, is perhaps doubtful, but it would be risky to discharge any patient before the face is thoroughly clean. I have found a lotion of weak bicarbonate of soda solution the best remedy for this condition, the face usually cleaning up comparatively rapidly if it is used daily. The buried crusts in the palms and soles are best removed on the point of a penknife, and in most cases shell out easily. Occasionally, however, instead of a hard crust, a small collection of sticky fluid is found which cannot be so easily got rid of. These collections are really like very small blisters lying in the skin, and should be laid open, the patient being instructed to soak the feet in strong antiseptics two or three times a day to disinfect the cavity. To wait for them to dry up would be too long a process.

Various attempts have been made to abort the eruption of small-pox. Of the different drugs which have been employed for this purpose I have personal experience only of one, *salol*. This, originally recommended by Begg, should be used from the moment the eruption makes its appearance, if any good result is to be obtained. When I have so used it, I have frequently noticed



SMALLPOX.

The crusting stage commencing on the face. The pustules on the arm are still unruptured. Note the scantiness of the eruption on the neck and upper part of chest.

that the eruption runs a rapid and short course, and that the pustules are imperfectly developed. But I have had to contend with the obvious fallacy that practically all the cases, in which I have had the opportunity of trying it, have been persons vaccinated in infancy, and we have already seen that in such individuals an eruption, which looks at first as if it was going to be very formidable, may suddenly and unaccountably abort without any special treatment. Such abortion, however, I am inclined to believe, I have seen much more often in cases treated with salol from the papular stage than in cases not so treated, or than in similar cases when the drug was first used after the eruption had become frankly vesicular. The doses given were 10 grains four-hourly. The treatment is quite a safe one, and in no way prejudices the chances of the patient's recovery, and is, I think, worth using in those patients who come under observation early. It would be also interesting to ascertain its effects in unmodified small-pox.

Denman reports successful results following the intravenous injection of *electrargol* in 10 c.c. to 20 c.c. doses. He has treated 150 cases of the confluent and semiconfluent type, and has markedly modified the case mortality. He states that, if treated before the full development of the eruption, the papules go no farther and there is no secondary fever. The injections are given daily for three or four days. It seems highly desirable that this important work should be confirmed.

Finsen has recommended that the patient be treated by *red light*. The colour red has had a traditional reputation in the treatment of the disease, red curtains and hangings having been used centuries ago. Finsen's treatment, however, depends on the absolute exclusion of actinic rays, which practically means treating the patient in a photographic dark room. Red glass for the windows and red shades for lamps are required, and as only a small proportion of ordinary small-pox patients come under treatment early enough for this method to be of any use, it is not an easy thing to adopt it in a hospital. Ricketts, who has experimented with it, does not regard it as of any value in aborting the eruption. His cases, however, were treated hardly early enough to constitute a fair test. Finsen considered that it is no use expecting results if the treatment is started after the fourth day of the disease. In other words, the patient must be placed in a dark room while he is yet in the early papular stage. It will always remain a difficulty that the patient usually does not reach hospital until the papules have become vesicular. Again, the difficulty of estimating the value of such a treatment in a population for the most part partially protected by vaccination in infancy, and therefore liable to abortion of the eruption in any case must not be underrated.

Vaccination has been recommended with the view of modifying the eruption after its appearance. Hanna, in his recent study of concurrent small-pox and vaccinia, thinks the operation should be performed on all cases admitted to hospital. Even if the eruption develops normally it is liable to dry up with astonishing quickness. Present views on vaccine-therapy make it seem quite probable that a vaccination, even if it does not 'take', may modify profoundly the course of the illness.

During *convalescence* there is no objection to the patient being allowed out in the hospital grounds. A liberal diet and, if the patient has been much weakened by the attack, such alcoholic stimulants as port wine or stout should be allowed. Frequent soap and water baths should be given.

Complications may be treated on the usual lines. The small boils and abscesses, so frequently met with in convalescence, should be freely opened. Their presence is usually an indication for the employment of some good general tonic; quinine has been highly praised in this connexion. Orchitis, during the course of the fever, should be treated with lead and opium fomentations and adequate support of the affected part.

Freedom from infection. The small-pox patient must be detained until the last crust separates from the skin. This, in mild cases, may be within three weeks; in severe, sometimes many months. From six to ten weeks is a very ordinary period of detention.

PROPHYLAXIS. On the outbreak of small-pox the first step to be taken is the prompt *isolation* in hospital of the affected persons. In the case of the other infectious diseases some latitude is usually allowed to those who can be satisfactorily isolated at home, but with small-pox this cannot be permitted. The next point of importance is the prompt *vaccination* of all contacts. The greatest care must be exercised in tracing all those with whom the patient has been directly in contact, as it is upon their effective supervision that the prevention of a large epidemic may depend. Should the outbreak be among the poorer classes, and more especially if the persons affected belong to the 'tramp' class, or live in common lodging houses, all contacts should be removed to a reception house, and there watched until the incubation period since their last exposure has expired. As successful vaccination in the incubation period is a possibility, it would be unwise to discharge patients a day or two before the end of it on the ground that the vaccination is 'taking'. The clothes of contacts should be disinfected with steam, and they themselves should receive disinfecting baths. Among the more respectable and settled population quarantine is not so necessary, and it will be usually sufficient for the houses to be visited daily by a competent inspector, who will report any appearance of illness among the persons

under observation. When vaccination has taken successfully these measures may be safely relaxed. Even for this slightly better class of contacts the use of the reception house is often advantageous, as detention for one or two nights allows of the thorough disinfection of their clothes, bedding, and homes. The *tracing of contacts* is nowadays regarded as highly important and may require a very large staff of inspectors. The advantage of tracing every one likely to have been even in momentary association with a patient in public vehicles or elsewhere was admirably shown by Davies in an outbreak at Bristol. The occurrence of thirty-nine cases of small-pox necessitated no less than 16,000 visits by inspectors, an expenditure of labour fully justified by the result.

Disinfection of the house is, of course, essential, and may be effected by the use of the formaline spray. It is safer to remove any old wall-paper and to thoroughly clean the walls and, in tenement buildings, to whitewash the staircases. All bedding and other fomites must be sent to the steam disinfecter. Apart from the risks to life which any omission of these details may entail, it must be remembered that small-pox, if allowed to become epidemic, may cause enormous expense to the community, and that it is cheaper in the long run to take very active measures from the first. Should, then, there be the slightest suggestion that the disease is going to spread, vaccination stations should be opened in suitable situations at convenient hours and free vaccination offered to the public. Leaflets, pointing out the advantage of obtaining efficient protection by this means, may also, with advantage, be distributed. The *notification of chicken-pox* is a highly desirable precaution when small-pox is epidemic. This brings to the notice of the Medical Officer of Health cases which otherwise might be missed altogether.

Small-pox hospitals and aerial convection. What is to be the situation of the Small-pox Hospital? In an adequately revaccinated community this is absolutely immaterial. In Germany the very existence of such buildings is unnecessary, and stray cases of the disease are nursed in general hospitals with no ill effect. In Great Britain, unfortunately, we have to provide accommodation for small-pox patients, and it is unquestionably advisable that the hospital site should be in a comparatively isolated situation. In 1881 Power demonstrated the influence of the hospital at Fulham on the population dwelling within a mile radius, and since then many other observers have noticed the greater prevalence of small-pox in the neighbourhood of small-pox hospitals during different epidemics. While this *hospital influence* may be said to be generally recognized, there are two distinct views regarding its nature. Power held that the infection is carried from the hospital by

the air. Others consider that defective administration on the part of the hospital authorities is responsible for the undue prevalence of the disease in the immediate neighbourhood. In the discussions on this subject each party has been able to produce a formidable array of sanitary experts in its favour, and, on the occasions on which the question has come into a court of law, the decision so far has been that the supporters of the aerial convection theory have not proved their case.

That infection can, under certain circumstances, be carried by air it would be unreasonable to doubt. The detached mummified crust from the palm of a small-pox patient is unquestionably capable of communicating the disease. It has been proved to cause a typical reaction when inoculated into the cornea of a rabbit, and it requires no great stretch of the imagination to conceive the possibility of such a scab being carried some distance in the air. How far its infectivity might be affected by prolonged exposure to fresh air or rain is a question of which as yet we know nothing. Nevertheless, the fact that, in many towns, the number of houses affected within a quarter-mile radius from the hospital has been shown to be considerably greater than that in the next quarter-mile of distance, and that this prevalence steadily decreases as we progress farther from the centre to more than the mile limit, strongly suggests that something of the nature of aerial convection exists in the neighbourhood of small-pox hospitals, and that this influence may make itself felt for at least a mile.

It must be remembered, however, that there are more ways of leakage of infection from a small-pox hospital than by air. However strikingly graded is the prevalence of the disease, as we increase our distance from the supposed centre of infection, the administration of the institution in question must be absolutely above suspicion before deductions of much value can be drawn. In some of the hospitals, on the experience of which the theory of aerial convection has been founded, there is no reason to doubt that the management was admirable; in others, again, also produced as evidence, the administration was not such as to exclude the possibility of infection being spread in a more tangible manner. Only those who have had experience of the recklessness of a certain section of the uneducated public as regards infection can realize what those possibilities may be. When the Edinburgh Small-pox Hospital was in the centre of the city it was necessary, not so many years ago, to have practically a cordon of police round its walls to prevent the outside public deliberately coming into contact with the patients. And, as regards a certain hospital in England, the Medical Officer of Health found that young men from outside were carrying on illicit amours, not only with the wardmaids, but actually with girls convalescing

from small-pox, and that within the hospital precincts. It is said that nowadays such breaches of discipline are impossible. It is certainly to be hoped so, but who can answer for every member of his staff?

But, whatever the cause, 'hospital influence' may be regarded as proved, at least in many instances,¹ and the Local Government Board of England requires that a small-pox hospital should not have a population of 600 within half a mile of it, even if some of that population is in an ordinary fever hospital. Fever hospitals, poorhouses, and other institutions are expressly forbidden within the half-mile radius. From my own experience in Edinburgh I am inclined to regard these regulations as unnecessarily severe. Our own small-pox buildings adjoin the Fever Hospital on the one side and the Poorhouse on the other, and the population within the quarter-mile radius is well over 1,500. No 'influence', however, has yet been observed.

The main and fundamental rule in administering such a hospital is to, so far as possible, prevent all coming and going. To secure this, I do not allow the nurses ever to leave the hospital grounds. They are sent over from the permanent hospital in their uniforms, are allowed to take no outdoor dress, and understand that they must be prepared to stay for at least six weeks. The grounds are spacious enough to secure ample facilities for exercise, and a week's holiday, after the term of service is over, is sufficient recompense for the imprisonment. In this way nurses, at all events, cannot spread the infection. In hospitals where nurses are granted leave it is necessary for them to have a disinfecting bath and to pass through a regular discharging house. The hair must be washed and disinfected, and drying boxes must be provided to dry it. Even with these precautions I think there may be some risk, as much must depend on the thoroughness with which they are carried out, and we all know the fate of pitchers which go too often to the well. Porters, again, should not be given leave, even though we fully realize the possibilities of their taking it. By strictly isolating the resident officials we reduce the dangerous staff to the visiting physicians and the ambulance attendants, of whom probably the latter constitute the only real danger. Every one who enters the wards must, of course, wear overalls and carefully disinfect the hands before leaving. No visitors should be allowed, except such clergymen as will submit to the regulations, and the relatives of absolutely hopeless cases. Vaccination must be enforced both on the staff and on visitors. Stores and food supplies should be deposited at the outer gates and from thence carried to the buildings by the hospital porters. It

¹ Those who desire to fully study this question are recommended to read the admirable paper of Dr. G. S. Buchanan, and the discussion which it elicited, as reported in the *Transactions of the Epidemiological Society*, vol. xxiv, 1904-5.

has been suggested that the systematic oiling of patients may limit the risks of infection being carried by air. I am a firm believer in the necessity of employing only the best officials of the nursing and domestic staff of the ordinary fever hospital for emergency small-pox work. Should extra officials be required, they should be utilized in the permanent hospital, and will thus set free nurses who are known to be trustworthy. Many small-pox hospital scandals depend, in my opinion, on the haphazard gathering together of an untried staff. For this reason, in particular, I think a distinct advantage is to be gained by having the temporary buildings of the small-pox hospital quite close to the permanent fever hospital, and not put far out into the country where efficient supervision is much more difficult. Modern fever hospitals are for the most part placed in comparatively isolated situations as it is, and, so far as my experience goes, the risk of the proximity of small-pox to them is overrated.

It is a somewhat melancholy reflection that it is only the extraordinary attitude of this country towards vaccination which renders this discussion of small-pox hospitals necessary. The whole question should be merely academic. As it is, it is unfortunately most practical.

CHAPTER VI

VACCINIA

Acquired Immunity from Small-pox.

Variolation.

Cow-pox: casual cow-pox, Jenner's discovery.

The Symptoms of Vaccinia in Man: local, general.

Generalized Vaccinia: accidental vaccinia.

The Nature of Vaccinia: Copeman's experiments.

The Value of Vaccination: influence on the

general mortality, attack rates of the vaccinated and unvaccinated, age incidence, case mortality, &c., &c., and effects of revaccination, immunity of hospital attendants.

Objections to Vaccination.

Vaccine Lymph and the Technique of Vaccination.

Concurrent Vaccinia and Small-pox.

Conclusion.

ACQUIRED IMMUNITY FROM SMALL-POX. Protection against small-pox may be acquired in one of three ways. Firstly, an *attack of the disease itself* will usually confer immunity against subsequent attacks. The degree of this immunity varies, for, as we have seen, second attacks of small-pox undoubtedly occur. It is, however, sufficient to modify very considerably the severity of the disease should it be again contracted. Secondly, *variolation*, or, in other words, inoculated small-pox, secures an amount of protection which is probably only slightly inferior to that conferred by an actual attack. Thirdly, *vaccination*, or the inoculation of cow-pox virus, gives, if practised sufficiently often, complete protection against the disease.

VARIOLATION. This process is of some interest, as the condition produced by it stands half-way in its symptomatology between small-pox on the one hand and vaccinia on the other, presenting features analogous to the general eruption of the one and the local reaction of the other. Otherwise its interest is merely historical, as it has been, quite rightly, forbidden by law. But in the days before vaccination, at a time when few persons escaped small-pox, it unquestionably had its advantages. Its object was to secure a mild and protective attack of a malady which was regarded as inevitable, and it can have required but little justification in an age when small-pox was so terribly destructive to life, vision, and good looks. The inoculation was usually made with a needle or lancet into the skin of the upper arm, and care was taken to use only the clear lymph from the small-pox vesicle, and preferably from that of the inoculated disease. About four

days after the inoculation a local reaction became manifest, papules appearing which gradually developed into clear vesicles. A stage of maturation followed, the pock becoming pustular on about the seventh day, by which time the surrounding skin was red and swollen and the patient suffered from considerable fever, which lasted till the tenth or eleventh day. During this fever subsidiary pustules formed in the areola round the point of inoculation, and such symptoms as headache, vomiting, and pain in the back were noticed. With the fall of the temperature on the eleventh day a generalized small-pox eruption appeared upon the other parts of the body and ran a fairly normal, if somewhat rapid, course. This eruption was practically always discrete, and was apparently in most cases analogous to the type now described as varioloid. It was, however, occasionally profuse and accompanied by severe secondary fever, and the illness in a small proportion of cases terminated fatally. It will be noticed that in this, the inoculated form of the disease, the incubation period is shorter than is the case in natural small-pox, and is more comparable to that of vaccinia.

It was customary to practise inoculation chiefly in children and young people, and precautions were taken that the patient should be in good health, and that he should not have been recently exposed to the natural disease.

The two disadvantages of the whole procedure are obvious. Firstly, it was occasionally followed by a fatal result. Secondly, while the disease which it provoked was usually of the type which we now describe as varioloid, it was, like varioloid, capable of causing unmodified small-pox in unprotected persons. The practice, then, was liable to assist in spreading infection, and infection of a possibly severe type.

COW-POX. This is an eruptive disease of the udder and teats of cows. It is infective and liable to spread among the cows in a dairy, the virus being carried on the hands of the milkers from animal to animal. Vesicles containing clear fluid appear on the udder, and these become surrounded with an area of inflammation. If ruptured, the vesicles form irregularly shaped ulcers and may develop into troublesome sloughing sores. The affected animal suffers in health. The fluid from a ruptured vesicle may infect any abrasion on the hands of the milker and what is called *casual cow-pox* is the result. This is a more severe form of infection than is observed in cases of ordinary vaccination, the difference, as Copeman observes, being probably due to the situation of the resulting vesicles and the purulent nature of the discharge from the sores on the teats. Large circular vesicles with a concave surface form on the hands, particularly about the joints and tips of the fingers. The surrounding parts become inflamed and indurated,

and the axillary glands may be enlarged and tender. Some degree of fever appears to be usually present. The vesicles ultimately either ulcerate or dry up, and the local inflammation subsides. There is no general eruption and the condition is not a fatal one.

The condition known as 'grease' or 'sore heels' in horses appears to be identical with cow-pox and can produce similar lesions in man. This *horse-pox* can manifest itself also as a pustular eruption in the mouths of horses, and Cameron has reported the case of a stableman infected from such a stomatitis.

It was apparently known before the time of Jenner that this disease of milkers gave some protection against small-pox. But to Jenner the whole credit of the discovery must be given, for it was he who first scientifically studied the question, and who brought the results of his experience before the public. The practice of variolation, which was then in vogue, gave him the opportunity of testing the protection given by vaccination against inoculated small-pox, and also of proving that the passage of the cow-pox virus through several human subjects did not affect its original protective power. His first paper, establishing the value of vaccination, was published in 1798. Unfortunately, however, he did not realize that the duration of the immunity conferred is limited. When, in after years, vaccinated persons began to contract the disease, doubts were not unnaturally cast upon the merits of the whole procedure. If from the first the necessity of revaccination after a certain time had been understood, it is unlikely that the question of vaccination would have ever caused the acute controversy which has raged more or less since its introduction.

THE SYMPTOMS OF VACCINIA IN MAN. After inoculation with vaccine lymph, with the exception of some irritation at the site of the abrasions for perhaps twenty-four hours, there are no symptoms for three days. This period of *incubation* is remarkably constant in primary vaccinations, though in rare instances it may be slightly longer or shorter. Raised, red, somewhat flat *papules*, then, appear at the site of scarification, and by the fifth day show distinct vesiculation. The *vesicles* contain clear lymph and are surrounded by a definite halo of redness. By the eighth day the vesicles have reached their full development and are usually plump and well filled, especially at the periphery, the centre being somewhat depressed. Vesicles which are close to each other tend to coalesce. It is at this period, if arm to arm vaccination is practised, that lymph is best taken for that purpose, and that the largest supply can be obtained for storage.

From the eighth to the tenth day is the period of *maturation*. The contents of the vaccine pock become cloudy, and ultimately yellowish and

purulent. There is now, as a rule, distinct inflammation of the surrounding skin, which becomes congested, tense, and of a deep red colour. This inflamed area is most distinctly raised above the level of the skin of the rest of the arm, but its edges are not defined, rather sloping away imperceptibly to the normal level. Occasionally the whole arm becomes red and swollen. In such cases there is every reason to suspect sepsis. The axillary glands may also become enlarged and tender. From the tenth day onwards a stage of *desiccation* sets in, the vesicle, whether ruptured or unruptured, slowly drying up and forming a crust, the inflammatory reaction subsiding at the same time. The resulting scab is usually deeply set in the skin and is firmly adherent. The time at which it finally separates and falls off varies much in different cases, but may be roughly fixed at between two and three weeks from the date of the vaccination. A pinkish scar is left behind, and this, as time goes on, becomes quite white and shows a well-marked pitted surface, or *foveation*. When vaccination is unsuccessful, occasionally a few abortive papules appear at the site of inoculation, causing a mulberry-like or nævoid appearance.

General symptoms are noted in many cases. These are best marked at the beginning of the second week, when the process of maturation is responsible for some fever. This is usually slight, but may be attended by headache, loss of appetite, sleeplessness, and general feelings of malaise. In young children, particularly, the sleep is often broken, and there is considerable gastric derangement, vomiting and so forth. If, however, the symptoms are at all severe, it will usually be found that there is more than a suspicion of sepsis in the wound. Apart from this fever of suppuration, there is sometimes an initial fever on about the fourth or fifth day after inoculation, and I have seen revaccinated adults suffer considerably from general malaise and slight fever about this period. At this time, too, erythematous rashes may be occasionally noticed in children. Maude and others have reported abdominal pain, sickness, and intense pain in the lumbar spine, especially in delicate women, and Hipsley reports that in the recent Sydney epidemic abdominal pain of an agonizing character was seen frequently in persons vaccinated from ten to fourteen days previously. He suggests the possibility of this being due to pancreatitis.

GENERALIZED VACCINIA. In a certain number of cases, besides the typical pocks on the arm, vesicles appear in other situations, notably round the nose and mouth. These are, as a rule, the result of scratching and auto-inoculation. It is interesting to note that, if a few days after vaccination the vaccine lymph is a second time inoculated, the lesions of the second inoculation develop so rapidly as to early reach the same stage as those of the first.

In addition, however, to auto-inoculation, it is beyond question that a general eruption of papules sometimes follows vaccination, usually at some time between the fourth and the tenth days. The eruption comes out in crops, and lesions in all stages of development may be observed at the same time. The individual spots, however, pass from the papule to the vesicle and pustule in the usual manner. The eruption is accompanied by some fever and may sometimes closely resemble small-pox. Why a general blood infection should occur in a few rare instances only is unknown. In the Australian epidemic generalized eruptions occurred in roughly 1 in 1,000 of persons vaccinated.

Accidental vaccinia. Just as a vaccinated person may by auto-inoculation spread the pocks over his own body, so he may infect other people in the same manner. Mothers attending to the arms of their recently vaccinated children occasionally inoculate themselves, and I have seen perfect vaccine pocks on the nose of a woman who contracted the infection in this manner. I have also seen the conjunctival surface of the eyelid inoculated in the same way, and the resulting condition notified as diphtheria.

THE NATURE OF VACCINIA. The fact that vaccinia affords such a marked degree of protection against small-pox, and the singular resemblance of the stages of development of its lesions to those of the true disease, are in themselves highly suggestive of the actual identity of the two conditions. This identity, however, has not been easy to prove. Nevertheless, several workers have succeeded, by the inoculation of small-pox material into calves, in producing, after transmission through several animals, typical vaccine vesicles, and the lymph so obtained has been used successfully for vaccination. In the first animals inoculated, however, typical vesicles are not produced, and the passage of the virus through a series of calves is necessary to secure results. In recent years Copeman, who had experienced great difficulty in his efforts to produce vaccine vesicles in calves with lymph from cases of natural small-pox, had the happy idea of inoculating the animals with the lymph of inoculated small-pox, and, variolation being illegal, was forced to produce the inoculated disease in the monkey. This animal is susceptible to small-pox, and, from the inoculation vesicles so obtained, Copeman secured lymph which after passage through several calves ultimately produced typical vaccine vesicles from which, again, children were successfully and typically vaccinated. From this he deduced that vaccinia is nothing more nor less than small-pox modified by transmission through the bovine animal. It has been stated by Kelsch that experiments of this nature are liable to be vitiated by the fact that the calves used for the test may be accidentally infected with vaccinia, but there is none the less every reason to accept them as accurate.

The researches of Councilman and his fellow workers have brought still further evidence of a histological nature in support of this conclusion. The results of the inoculation of vaccine and small-pox lymph on the cornea of the calf and rabbit have been found to be identical, and the cell inclusions, regarded as typical of small-pox, have been found in the lesions.

THE VALUE OF VACCINATION. Assuming the practical identity of the two conditions, however highly modified a form of the disease vaccinia may be, it is reasonable to expect a protective influence against small-pox to be exerted by the practice of vaccination. But we now have to briefly consider the evidence on which we base our claim that by universal vaccination and revaccination it would be possible to prevent the occurrence of small-pox altogether. Without entering into elaborate statistical details of this evidence, which are entirely beyond the scope of this volume, it will be sufficient to mention a few of the salient facts which, considered either separately or together, all tend to prove the value of vaccination and the importance to the community of its enforcement.

Firstly, then, there is the marked *fall in mortality* from small-pox, dating from the introduction of vaccination. This has been noticed everywhere where comparative returns of the number of small-pox deaths are available. Commencing with the year 1801 the mortality in London and in the best vaccinated continental countries showed a steady decline for a number of years, rising again slightly—and this is a significant fact—about twenty years later, by which time there would be obviously a large number of persons requiring revaccination. The introduction of vaccination by the Americans into the Philippine Islands has been followed by an extraordinary reduction in the mortality from small-pox, which, formerly exceptionally prevalent, is to-day for the most part limited to very outlying districts.

Secondly, vaccinated persons suffer from small-pox in a much smaller proportion than do the unvaccinated. At a time when only 10 per cent. of the children of London were unvaccinated, of 2,863 patients under ten years of age admitted to the Homerton and Fulham hospitals with small-pox, no less than 46 per cent. had never been vaccinated. The unvaccinated population, then, yielded for its numbers nearly five times as many cases of small-pox as the vaccinated. Similar evidence may be obtained by studying the *attack rates* of the vaccinated and unvaccinated population of houses invaded by small-pox. Persons living under the same conditions as regards surroundings, food, and sanitation show a marked difference in their susceptibility to small-pox, according as they are vaccinated or not. Thus McVail, analysing the experience of Warrington, Dewsbury, Gloucester, and Leicester in this respect, shows that at all ages the vaccinated population of the

invaded houses had a much lower attack rate than the unvaccinated, and the distinction between the two classes becomes more marked when the susceptibility to the disease of children under ten years of age is alone considered. At Warrington, for instance, only 4·4 per cent. of the vaccinated children exposed were attacked, as against 54·5 per cent. of the unvaccinated. At Dewsbury as many as 10 per cent. of the vaccinated contracted the disease, but of the unvaccinated, on the other hand, 50 per cent. suffered. The experience of the other towns mentioned was of the same nature.

Thirdly, since the introduction of vaccination the *age incidence* of small-pox has entirely changed. Originally the disease resembled measles. Nearly every one took it in early life, although, like measles, it was equally liable to attack an older person who was not protected. When, however, most children were submitted to vaccination, sufficient protection was conferred on them to postpone the liability to attack to many years later, and thus we find to-day, in communities in which infantile vaccination is practised, but in which there is no systematic revaccination, that the vast majority of our small-pox patients are adults. But, even to-day, in those towns which have made themselves remarkable as antivaccination centres, the age incidence of the disease exactly resembles that of the prevaccination times. At Gloucester, for instance, 64 per cent. of the persons attacked in the last epidemic were children of under ten years of age; this in a town in which, just before the outbreak, the percentage of vaccination default had reached the astonishing figure of 85 per cent. Contrast this with the experience of well-vaccinated Glasgow in 1900, where out of 1,730 patients only 96, or 5·5 per cent., were children of under ten years, and of this 96 it need hardly be added that a large proportion, 62, had never been vaccinated.

Fourthly, we have to consider the great difference in favour of the vaccinated in the *mortality of those attacked*. We have seen that, while revaccination may be necessary to secure complete protection from small-pox, vaccination in infancy lessens considerably the chances of a fatal issue, should the disease be contracted. To take the recent epidemic of 1900-1 as an example, of 9,659 cases treated in the London hospitals of the Metropolitan Asylums Board, 11·5 per cent. of the vaccinated, and 33·1 per cent. of the unvaccinated, died. In the Glasgow Fever Hospital the mortality was 10·4 per cent. among the vaccinated and 51·6 per cent. among the unvaccinated.

This difference in mortality may be accentuated if we consider whether vaccination, as evidenced by the marks existing on the patient, has been really efficient or not. The mortality varies with the number of the marks, the character of the marks, and the superficial extent of the marks. As

regards number, the patient with two marks has, roughly speaking, a better chance of recovery than the patient with one; those, again, with three or four marks being still less likely to succumb. Thus, of 11,724 cases treated in the Metropolitan Asylums Board Hospitals, the percentage death-rate of those with one mark was 13·5, with two 8·4, with three 6·4, and with four or more 3·8. A good mark differs from a bad mark in showing a definitely foveated surface. If only the patients with good marks in the above figures be counted, the percentage mortality was 6·4 for one mark, 3·7 for two and three, and 2·7 for four or more. As regards the superficial area of the marks McCombie found that, if one-third of a square inch of well-foveated surface be held to constitute efficient vaccination, of 1,435 patients showing efficient vaccination 2·5 per cent. died, whereas of 4,375 patients showing imperfect vaccination 8·7 per cent. died.

Not only does the actual mortality of the two classes differ, but the *severity of the attack*, as judged by the amount of the eruption, is much greater in the unvaccinated. In the last Glasgow epidemic 56 per cent. of the unvaccinated cases were either confluent or hæmorrhagic, that is to say, of a very severe type. Of the vaccinated cases, only 19 per cent. suffered from these severe forms of the disease. My much more limited experience in Edinburgh at the same time was to the same effect. Of the vaccinated cases, 28·9 per cent. were varioloid or modified, 55·8 per cent. discrete, and 15 per cent. confluent or semi-confluent. Of the unvaccinated, only 9·5 per cent. were varioloid, 33·8 per cent. discrete, and 57 per cent. confluent or semi-confluent. It will be noticed that the last figure tallies almost exactly with the Glasgow percentage.

Fifthly, the admirable results obtained by systematic *revaccination* are perhaps the most striking proof of the protection which can be secured if full advantage is taken of Jenner's discovery. In Germany, since revaccination has been enforced, small-pox has been almost unknown. The few individuals who contract it are for the most part foreigners who have not been revaccinated. That there are many opportunities for the disease to be introduced from less well-vaccinated countries cannot be doubted, and yet it is not even necessary to maintain small-pox hospitals. Contrast Berlin, with its twelve beds for small-pox in a pavilion of a general hospital, with London, with its 2,500 beds in hospitals specially constructed and maintained for small-pox alone. The German law insists on revaccination at school age, and the male adult population is again revaccinated on entering the army. In this country, also, those classes which have to undergo revaccination, such as soldiers and postmen, have been proved during great outbreaks to have been practically free from the disease. We also have the example of

small-pox hospital attendants. The Vaccination Committee of the Epidemiological Society found that of 734 attendants employed in hospitals of the Metropolitan Asylums Board, 79 had had small-pox and 645 had been successfully revaccinated before undertaking duty. None of these took the disease. The remaining ten had not been revaccinated, and all contracted small-pox. The only Edinburgh City Hospital nurse who contracted small-pox in the last forty years was also the only nurse who refused revaccination. Since I have been connected with the hospital I have always made it a rule that every attendant must be revaccinated on commencing duty, and I have had no accidents.

The above facts, then, are amply sufficient to justify compulsory vaccination. Those who desire fuller information are advised to read Dr. McVail's very complete account in Clifford Allbutt's *System of Medicine*. Some of us are perhaps even more impressed with individual cases seen by ourselves than by monumental masses of figures. I remember an old woman who alone, of the numerous population of a crowded tenement infected with small-pox, absolutely refused revaccination. She alone took the disease and died of it. Again, when we see babies, brought with their mothers into hospital, because there is no one at home to look after them, after vaccination on admission remain for weeks scatheless in the wards, we cannot fail to be impressed. My own experience of nurses is that a certain proportion will take the infectious disease which they are nursing. Each year sees some of our nurses down with diphtheria, scarlatina, measles, or enteric fever. When typhus appears, one or two nurses invariably take it. Small-pox alone is an absolutely safe disease to nurse. No heroism is required, repulsive as the work is. The revaccinated nurse is perfectly protected.

OBJECTIONS TO VACCINATION. What, then, are the objections to vaccination? The first undoubtedly is 'that it doesn't protect'. Some persons, no doubt, will never be convinced. Secondly, it is said to be dangerous, to cause erysipelas, skin diseases, syphilis, and so forth. It is obvious that, if great care is not taken to perform the operation aseptically and to keep the subsequent wound clean, erysipelas and septic infection are certainly possibilities. There is no reason to believe that skin diseases are caused by vaccination. As regards syphilis, the possibility of the lymph from a syphilitic child being used must certainly be considered, but public vaccination is now invariably performed with calf lymph, and such lymph should always be used. Lastly, there is the objection to the idea of compulsion, the interference with the liberty of the subject. As Goodall well points out, if vaccination is not practised, the only alternative method of preventing the spread of the disease is by compulsory isolation and

quarantine. It appears, then, that the last state of the 'subject' would be, as regards his liberty, worse than the first.

Dr. Killick Millard's view of compulsory vaccination is an interesting one. He holds that persons partly protected by infantile vaccination are liable to get the disease so lightly that it often remains unrecognized, and that its dissemination is therefore actually facilitated. But this is no argument against a really compulsory system which should certainly include revaccination at suitable periods. It is, in fact, the neglect of revaccination which is responsible for the existence of a controversy on the subject.

The commonly advanced argument that the greater rarity of small-pox since the introduction of vaccination can be accounted for by improved sanitation is by no means convincing. The other disease from which very few unprotected persons escape and which, like small-pox, in the old days, is particularly common among children, is measles, which unfortunately, in spite of all improvements in housing and sanitation, is as destructive to-day as it ever was.

VACCINE LYMPH AND THE TECHNIQUE OF VACCINATION.
Difficulties of storing calf lymph and of keeping up a supply that should be at once pure and efficient, originally led to public vaccinations being always performed with human lymph. This practice was discontinued in 1899, and now glycerinated calf lymph is practically universally employed. The admixture of glycerine has the advantage of destroying all the ordinary saprophytes found associated with lymph, and the mixture is even more efficient as vaccine than the original lymph. The common practice is to inoculate with glycerinated lymph a calf which has been previously submitted to the tuberculin test. The inoculations are made on the shaved skin of the abdomen, precautions being taken to avoid any chance of sepsis. Ninety-six hours later the epithelium and underlying vesicular pulp are removed with a sharp spoon, and the scrapings collected and weighed. Four times its weight of a sterilized 50 per cent. mixture of pure glycerine and distilled water are then added, and the whole is ground up in a mortar. The resulting emulsion is stored in a cool dark place, and is ultimately drawn up into sterilized capillary tubes for distribution. In India and tropical climates lymph is likely to deteriorate, and vaccinations are best performed in the cold weather. James recommends the storage of vaccine in thermos flasks.

The ordinary method of vaccination is by scarification. This may be done with a needle, a blunt lancet, or with one of the scratching instruments invented for the purpose. I personally always use a four-pronged, somewhat blunt-pointed, metal scratcher, made all in one piece with its handle. It must be remembered that the same care should be exercised in vaccination

as in any minor surgical operation, and whatever instrument is used should be scrupulously cleaned and sterilized first. When a series of revaccinations are being done at the same time, passing the instrument through the flame of a spirit lamp and washing in sterilized water is the handiest method. Or a large number of needles can be kept ready boiled. The arm should be carefully cleaned with soap and water first. Afterwards I usually scrub it freely with weak carbolic lotion and then wash off with plenty of sterilized water. Scarifications may then be made in two or more places, the usual position being at the insertion of the deltoid muscle. If only two marks are made they should be large ones. The usual practice is to make four for a primary vaccination, and this should be insisted on. With anxious parents, however, it is perfectly easy to make only two marks and yet include a larger total area. The scarification is best made through a drop of lymph placed on the skin. The scratches should not draw blood, but they should be deep enough to show a little pink. It is better not to make them across each other, but all in the same direction. Otherwise there is unnecessary loss of tissue from necrosis of minute areas of skin, an ugly scar, and no more efficient vaccination than if the lines were parallel, and all in the same direction. The marks should not be placed too close to each other for the same reason. The greatest care should be taken to keep the arm clean. Shields should not be encouraged, but a plain pad of antiseptic wool may be applied to the arm. A dusting powder of boracic acid and starch is useful to keep the pocks dry, and it is most advisable that they should not be broken. There are some advantages to be gained by vaccinating healthy babies when they are very young. They can, when under a month old, use their arms so little that the wound is kept immobile, and there is little chance of extraneous irritation. They also seem to suffer much less than at a later age.

When due precautions have been taken with regard to asepsis, it is wonderful what perfect pocks can be obtained with little or no areola of redness. The inflammatory reaction must almost certainly be due to other causes than the vaccine itself. It is hardly necessary to emphasize the importance of care in the performance of vaccination and in the subsequent treatment of the arm. Much of the prejudice which so unfortunately exists is undoubtedly due to the reckless way in which this little operation is so often done.

CONCURRENT VACCINIA AND SMALL-POX. Not only does vaccination protect against an attack of small-pox, but it undoubtedly also will, if performed in the early days of its incubation period, prevent its development in persons already infected. Any one, indeed, who is revaccinated within three days after a single exposure to small-pox may be regarded as practically safe. Hanna has, however, collected two or three

instances of persons vaccinated on the second day after presumed infection who developed mild small-pox as well as typical vaccinia. Armstrong reports that of the small-pox cases in Sydney one only was successfully vaccinated eleven days before the onset of symptoms and three eight days before. The incubation of small-pox being several days longer than that of vaccinia it is easy to see how in some cases the latter has time to reach its full development and exert its protective effect before the former has a chance of appearing. But, if the vaccination is not performed too late, it may still have a distinctly aborting effect on the course of the small-pox, even though it has failed to prevent its occurrence. Vaccination has been reported to have been performed successfully at all times during the incubation period. I have seen several cases in which it was done three or four days before the commencement of an attack of small-pox, and ran a course coincident with the small-pox eruption. In one case the patient was vaccinated on the first day of her symptoms, and the vesicles developed normally. The small-pox eruption was in this case confluent, but the patient's condition never gave any anxiety, and the constitutional symptoms in no way tallied with what might have been expected from the severity of the eruption.

CONCLUSION. By the practice of vaccination and revaccination it is quite possible to banish small-pox from any given country. Revaccination should be performed at about the age of ten years, and again in adult life. Those who are likely to be exposed to the disease should not trust a successful revaccination of more than five years' standing. I say successful, as if it has been unsuccessful there is no proof as to how long the immunity may have lasted, and revaccination must be attempted again at the first chance of exposure. It would be unsafe to wait in such a case as long as five years. An unsuccessful vaccination, however, when performed by a competent person, and with lymph which is giving successful results in other persons, may be regarded as proving immunity against small-pox for the probable duration of any outbreak. Hospital attendants, however, it is advisable to revaccinate a second time, if the first attempt fails. Welsh, in a recent study of the question in the Sydney epidemic, states that occasionally a vaccination which has been unsuccessful succeeds when performed again about ten days later. He suggests that this is due to sensitization, and that therefore second attempts made at this period are more likely to be successful than those made earlier or later. It is highly important that our hospitals should be spared the disgrace of contributing to the number of small-pox patients. It seems probable that in the meantime we shall have less to fear from small-pox than usual. The general revaccination practised on men of military age will prove a very great protection.

CHAPTER VII

CHICKEN-POX

Introduction.	Complications.
Etiology: predisposing factors.	Severe types.
Infection and Dissemination.	Diagnosis.
Period of Incubation.	Prognosis.
Period of Eruption.	Treatment.
General Symptoms.	Prophylaxis.
Second attacks.	Relationship of Chicken-pox to Herpes.

Synonyms—Varicella, Crystal Pox. *French*, Varicelle. *German*, Wasser-pocken.

INTRODUCTION. Chicken-pox, contrary to the opinion of Hebra and other distinguished writers, is unquestionably a perfectly distinct disease from small-pox. This is proved by the fact that it leaves behind it no immunity against either small-pox or vaccinia. And in the same way neither of these two conditions confers any immunity against chicken-pox. Instances of this want of acquired protection have been frequently observed in small-pox hospitals, patients, who in reality were suffering merely from chicken-pox, being accidentally admitted, and thereafter contracting the more severe infection. Such an introduction of chicken-pox into the wards has also been followed by instances of it infecting the small-pox convalescents. Moreover, during the course of an epidemic of chicken-pox we find that the disease 'breeds true'. Under no conditions does it give rise to cases of small-pox. Contrast this with varioloid, the form of small-pox with which it is most likely to be confused, and which is capable of producing the most severe types of true variola in unprotected persons. As apart from these important points, there are many features of difference between the two diseases of a purely clinical nature, as will be seen when their differential diagnosis is discussed.

ETIOLOGY. There is no reason to doubt that chicken-pox is the result of infection by a micro-organism, and it is possible that that micro-organism may be found to be a protozoon. But, so far, we have no evidence as to what is the cause of the disease. It is true that de Korte has described unicellular organisms, with amœboid movement, as occurring in the clear

fluid of the vesicles, and considers that they are concerned with the causation of chicken-pox. But, on the other hand, Tyzzer, who investigated the histology of the lesions, found no definite evidence of parasites such as those which he believed to be the cause of small-pox and vaccinia. In the meantime, then, we must be content to await further researches.

Predisposing Factors. Chicken-pox is a very widely disseminated disease. It is endemic in most large cities and, at times, shows an epidemic prevalence. It is not much affected by *season*, but is probably more liable to occur in large outbreaks in the autumn months. As the disease is not notifiable it is difficult to obtain reliable statistics regarding sex and age incidence. To judge, however, from the records of the city of Basel, in which some form of notification seems to exist, *sex* exercises no influence. As regards *age*, on the other hand, the vast majority of cases occur in the first ten years of life. Thus of 6,014 cases reported in Basel from 1875 to 1906, no less than 5,771 were under ten years of age and only three were over forty, one of these being over fifty years. For a long time distinguished German clinicians, especially Senator and Henoch, questioned the possibility of chicken-pox occurring in the adult, but this view has been abandoned by recent German writers and is, of course, quite an untenable one. Most persons are protected by an attack in early life, and this fact, as in the case of measles, makes chicken-pox in the adult comparatively rare, while it is not improbable that increasing age confers some degree of protection also. The Basel statistics show twenty-four patients of over twenty years, a very small number out of 6,000 it is true, but undoubtedly giving a very much more fair estimate than my own figures, which for the last 458 patients sent into hospital as chicken-pox include forty cases of over twenty years. Chicken-pox, as such, is seldom isolated in hospital and, as is the case with rubella, soldiers, sailors, students, nurses, and adult lodgers in hotels and so forth are liable to be admitted in an undue proportion. I have seen only three patients of over thirty-five years of age with the disease, but McCombie has had a patient of seventy years of age. Infants of under one year often escape, but 691 cases, or about one tenth of the whole, were notified in Basel.

INFECTION AND DISSEMINATION. Chicken-pox is highly infectious. In this regard it ranks with measles and small-pox. The contagion is usually communicated directly from person to person, but can be carried short distances by intermediaries, as for instance nurses in a ward full of children. While it appears to me very doubtful if it can be transmitted by *air*, Foord Caiger is strongly of opinion that infection can occur by such means, and for this reason considers the disease as unsuitable for 'cubicle'

isolation. The recent work of Frederic Thomson on 'bed isolation' points to the same conclusion, but I am none the less inclined to the belief that, with so highly infectious a virus, the slightest omission in technique on the part of the nursing staff would be apt to cause disaster, and, with full appreciation of the wonderfully successful results obtained by specially selected nurses in the case of other diseases, consider that human fallibility, as well as the possibility of aerial convection, must be allowed for. The virus is probably short-lived in clothing or other *fomites*. It is doubtless inhaled by the infected person. The disease is perhaps chiefly spread by the aggregation of small children in infant schools. The infectivity, although as stated above usually high, is occasionally very slight, and in one year I have seen six importations of incubating cases admitted to a large ward, always full of very young children suffering from whooping cough and nearly all susceptible, followed by no instance of infection. Usually, however, such an importation causes the outbreak of several secondary cases even if the patient is removed on the appearance of the first spot. Chicken-pox, indeed, is infectious from the first moment of the eruption and may well be so earlier, at any rate in those cases which present a definite, if short, prodromal stage. Thomson's careful observations go far to show that the infectivity declines very rapidly, and he seems to doubt whether it really continues, as is generally held, until the last crust has separated. I am, however, only able to account for occasional mysterious outbreaks of the disease, at times when there has been no case in hospital for months, on the supposition that some patient has been admitted with one or two undetected crusts on the scalp or elsewhere, and from the analogy of small-pox it would at least be reasonable to assume that the scabs are dangerous. On the other hand, a recent experience has made me wonder whether infectivity may not in exceptional instances outlive even the crusts. A boy, admitted with concurrent chicken-pox and scarlet fever, was, after three weeks isolation and the separation of the last crust, transferred to a scarlet fever convalescent ward, his clothes having been disinfected by steam and his personal disinfection having been carefully attended to. An outbreak of three cases occurred from fifteen to seventeen days after his transference, although all the children affected had been over three weeks in hospital when first exposed to him and did not all come from the same acute ward. No other source of infection could be detected.

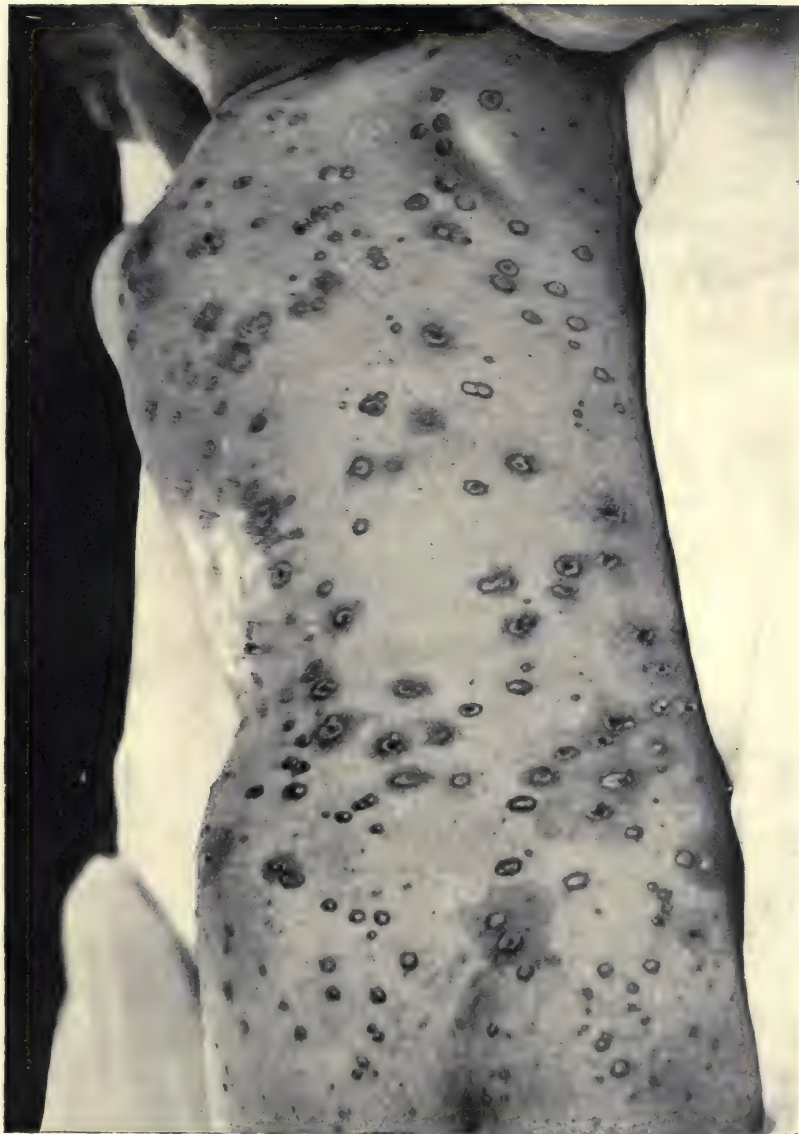
Attempts to induce chicken-pox by *inoculation* appear for the most part to have failed. Kling, however, has recently reported a series of interesting experiments to secure a protective inoculation. He used the contents of a perfectly clear varicella vesicle and inoculated it, as in vaccination, into

the arm. About the eighth day papules appeared at the site of inoculation, to be followed twenty-four hours later by typical varicella vesicles. In a few instances a doubtful scanty papular eruption appeared on the body a few days after inoculation, which was regarded as probably an abortive attack of chicken-pox. Kling believes that inoculation confers a considerable amount of protection. Of thirty-one children treated only one took the disease, although all were exposed. The experiments, nevertheless, are of but little practical interest, as chicken-pox is too trivial a condition to justify preventive measures of this type.

PERIOD OF INCUBATION. The extreme limits of this period, as judged from the careful observations of Brownlee, would appear to be eleven and twenty-four days respectively. None of my own cases, however, have taken less than twelve or more than twenty-three days to develop. Common days for the appearance of the first symptom are the thirteenth, fourteenth, fifteenth, and sixteenth, and somewhat less frequently the seventeenth. Incubation periods lasting up to nineteen days are not unusual. After that interval has elapsed since the moment of exposure, I have very seldom seen the disease develop, and I can recollect only one or two cases in which the period was as short as twelve days. I think that a latent stage lasting more than three weeks must be extremely rare, as after twenty-three years' experience of several outbreaks annually in one or other of our wards, I have found that a twenty-two days' quarantine for the patients in an infected ward has been sufficient except on one occasion.

STAGE OF INVASION. If this stage is, as is customary, held to last from the moment of the first symptom to the appearance of the eruption, it may be said that in a very large number of cases—the great majority in fact—it is wanting altogether. The skin eruption, indeed, is usually the first symptom of the illness, particularly in children. But in some cases a well-marked invasion stage does exist, and occasionally it is even severe. It may vary from merely slight malaise and 'crossness' in children lasting for a few hours to a well-defined fever of two days' duration. The latter, no doubt, is rare, but some pyrexia, well-marked headache, shivering, and general feelings of discomfort are not uncommonly noticed, especially in adults, for twelve to twenty-four hours before the eruption appears. It is highly important that the possibility of the occurrence of such prodromal symptoms should be thoroughly recognized, as otherwise a case might be too readily regarded as one of small-pox. Even pain in the back may be sometimes, if rarely, complained of.

Even if the prodromal symptoms do not last so long as twelve hours they are occasionally sufficiently well marked. Vomiting and gastric dis-



THE LESIONS OF CHICKENPOX.

Note the oval shape and irregularity of margin of these exceptionally large vesicles.

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turbances may occur in children. In rare instances the appearance of the eruption is preceded by high fever and severe convulsions. I have seen an interesting example of an onset of this kind. Being, when in general practice, called to see a child in a fit, I found that the temperature was 105° and that there was no rash of any kind. Shortly after placing the child in a hot bath, with mustard in the water, clear chicken-pox vesicles appeared profusely all over the trunk, and by the time the patient was removed from the bath the convulsions had ceased and the diagnosis was beyond all question. The temperature fell rapidly, and the fits were not repeated, the subsequent course of the case being quite uneventful.

An interesting feature of the prodromal period is the occasional occurrence of erythematous *rashes*. These vary in appearance, being sometimes urticarial, sometimes morbilliform, but for the most part they resemble the rash of scarlatina. My own experience is limited to these scarlatiniform rashes, which are not at all uncommon during the course of chicken-pox, and which, when occurring in the stage of invasion, are apt to lead to error in diagnosis. I have seen them both with and without pyrexia. The patient may present a more or less uniform flush, or there may be an actual punctate rash. The trunk is the most common situation, but occasionally the limbs are also involved. The fauces may be markedly injected. There is no subsequent desquamation. Two or three cases every year are sent into the Edinburgh City Hospital, notified as scarlatina, which on admission present only early chicken-pox vesicles. These vesicles, no doubt, were not visible at the time when the patient was seen by the general practitioner, but, on the other hand, it is only fair to assume that a rash resembling closely that of scarlatina must have been present to justify the notification. The experience of other fever hospitals is similar, and it may be safely concluded that the scarlatiniform prodromal rash is not a very rare feature of the chicken-pox invasion.

STAGE OF ERUPTION. When the eruption can be watched from its first appearance it is often possible to trace it through macular and papular stages before the typical vesicle is formed. The macule is no doubt a very transient stage, but the papule may last for some hours and is not unlike a typhoid spot in its appearance, being pink, slightly raised, and readily disappearing on pressure. The *vesicle*, however, forms exceedingly quickly and in some cases seems to be the first manifestation of the eruption. At first it contains perfectly clear fluid, so clear, indeed, that, as the covering pellicle is extremely thin, some patients appear to be covered with scattered drops of water. In shape the vesicle is either circular or oval, elongated forms with somewhat irregular margins being often met with. It lies rather

on than *in* the skin, and the more superficially it lies the more apt is it to assume oval and irregular shapes. On the scalp, and extremities, and particularly on the forearms, hands, or feet, it is more definitely circular and more deeply set in the skin, being quite hard to the touch in these situations, and sometimes definitely 'shotty'. On the trunk, however, the lesions are usually soft and velvety to the touch. The roof of the vesicle is rounded and more or less dome-shaped. Occasionally a narrow and somewhat pale areola surrounds the spot, but often the surrounding skin is quite normal in appearance, and in such cases particularly the suggestion of drops of water is well marked. It is usual to describe the vesicle as unilocular. This is clinically correct in so far that it collapses when pricked with a needle. Histologically, however, septa exist, but they apparently rupture easily with the increase of growth of the vesicle.

As the vesicle grows older, if it remains unruptured, its contents become distinctly cloudy and pearl-coloured, and ultimately, in some few instances, actually purulent. The majority of vesicles, however, have but a short existence, as they are very liable to early rupture, either from the rubbing of the clothes or from the patient scratching them. Few probably remain unruptured for more than two days. Even these are often of a badly developed type, containing but little fluid, and often resembling half-empty blisters. If rupture, on the other hand, occurs, the contents either completely or partially escape. In the former case the emptied vesicle rapidly dries up and a superficial crust is formed; in the latter, a small scab may form in the pellicle of the vesicle at the point of rupture, and by fixing down, as it were, the centre of the pock may prevent any further escape of the contents. As a result of this we have an appearance of umbilication, the centre of the vesicle being depressed, whereas the periphery is often distended with fluid which by this time is apt to be purulent. The depression, however, is by no means always central; it may be at one end of an elongated vesicle or somewhat nearer one margin than another, and there is always some suggestion of a scab in the umbilicated part. Such vesicles either rupture a second time, or gradually desiccate, the central crust increasing in size. The crusts are dark in colour, and often consist largely of coagulated blood, if the lesions have been much scratched. In shape they follow the outline of the original vesicle. They lie more superficially than the crusts of small-pox, but if there has been much septic inflammation of the floor of the vesicle they may be deeply set in the skin, and on separation leave an ugly mark behind them. They are occasionally buried in the tough skin of the palms and soles exactly as are those of small-pox. The scar, which is at first a dirty pink colour, becomes ultimately white. It is not foveated, the destruction of the skin not

having reached deep enough levels to cause that appearance. It remains as a recognizable mark for life in a certain number of cases, its oval or irregular shape proclaiming its origin. Only after gangrenous cases is it puckered or depressed.

So much, then, for the life history of any given lesion on the skin from its first appearance. We now have to note that the vesicles appear in *successive crops*. This is one of the main peculiarities of the eruption and distinguishes its behaviour from that of small-pox. New vesicles may appear daily, for two or three days only in slight cases, for a week or more in those which are more severe. Each papule, on its appearance, passes through its successive stages in its own time, some, from the early rupture of the vesicle, drying up rapidly with crusts, others remaining unruptured for two or more days. The crusts, again, in some places fall off early, in three or four days from their formation, and in other places, owing to the skin being more deeply involved, remain attached for as many weeks, or even longer. At a very early period, then, in the course of an ordinary case, the skin presents a large number of lesions in all stages at the same moment. Papules, vesicles, pustules, crusts, and even the stained mark left by the separation of a crust which has fallen off early, may be seen side by side on quite a small area of skin.

In the vast majority of cases the vesicles appear first on the trunk. Sometimes, indeed, the trunk alone presents any eruption. I have for the last ten years paid particular attention to the *distribution* of the chicken-pox eruption, but although, broadly speaking, it has fairly definite characteristics, it is much more irregular and less constant than that of small-pox, and it must therefore be described with certain reservations. We may state as a general rule that the trunk is most affected, then the face and scalp, the extremities least of all. It is true that in profuse eruptions numerous spots may be seen on the hands and feet and even on the palms and soles, but in a great majority of cases the forearms, wrists, and hands suffer very little, and, not at all infrequently, are absolutely free from lesions. The same is true of the legs, though they may be found to be spotted even when the arms have escaped altogether. The eruption is seen at its best on the back, and is usually most profuse in that situation. The flanks are well spotted and the axilla is often invaded. The mucous membranes of the mouth are frequently affected. Vesicles may be seen on the palate, usually surrounded with a deep red areola, and often rupturing early and leaving a greyish-coloured ulcer behind them. The vulva may also be implicated.

As is the case in small-pox, any condition causing skin irritation may modify the distribution of the eruption. The spots may be disproportionately

numerous, for instance, in the region covered by the napkin in infants. I have had under my care a boy whose clavicle was fractured during the incubation period, and the shoulder, arm, and forearm, as well as the side of the chest, which had been covered with the bandage, presented a spotting at least three or four times more profuse than that on the unaffected side. Another recent case, a young lady who had very typical discrete chicken-pox lesions on the body, showed on her face such a profuse and closely-set eruption that she gave quite the impression of small-pox, especially as the brow and prominences of the face were much more affected than the less salient parts. This was easily explained by the fact that she had just returned from a week end in the country, where she had spent her time sitting in the sun, and the irritation of the sunburn had determined the localization of the eruption. Another patient, who developed his chicken-pox only four days after an intense scarlet fever rash, had an unusually copious eruption on the trunk and extremities, and yet had only three or four spots on the face. This suggested that, had the fever not occurred during his incubation period, he would probably have had a very scanty eruption, but the skin hyperæmia caused it to be profuse on the trunk and limbs, whereas the face, spared by the scarlet rash, presented as it were more resistance.

As regards the profuseness of the eruption, it is, as a rule, very discrete, considerable areas of unaffected skin lying between the lesions. In one of my cases the whole eruption was represented by one typical vesicle on the lower part of the abdomen. The patient had been exposed to chicken-pox, and two other children in the same ward developed the disease on the same day, so that the diagnosis was beyond all question. To go to the other extreme, occasionally patients may be seen in whom the eruption is so profuse that it would be impossible to lay the tip of a finger on the back without touching two or more vesicles. In such well-marked cases we must expect a copious eruption on the face and extremities also. Occasionally even small areas of confluence, due to the blending of several vesicles, may be noted. But the average case presents an eruption consisting of lesions which, even on the trunk, are two or three inches from each other.

GENERAL SYMPTOMS. The *temperature* may or may not be raised. As we have seen above, the first symptom of the disease may be the appearance of the eruption. In such cases, unless it is very profuse from the first, the pyrexia may be delayed for two or three days, and only appears when the vesicles suppurate, being in this way reminiscent of the secondary fever of small-pox. Other patients may show a slight temperature, 99° to 100° F., for the first couple of days, and this may rise later to higher levels as the eruption develops (Fig. 26). In others, again, the temperature remains

normal throughout the whole course of the illness, or is only slightly elevated for one or two days. The course of the fever in a sharp case is shown in the chart (Fig. 27). It will be noticed how the temperature rises as the eruption continues to come out, reaching its full height some days after the onset. The *general symptoms* are usually in direct proportion to the amount of fever. If the pyrexia is absent or slight, the worst the patient has to suffer is the skin irritation. If it is well marked, headache, insomnia, loss of appetite,

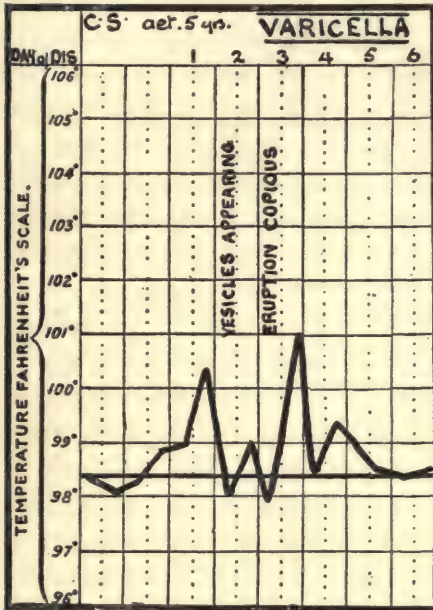


FIG. 26. A case of chicken-pox, showing some preliminary fever and the slight irregular pyrexia usually seen in the average patient.

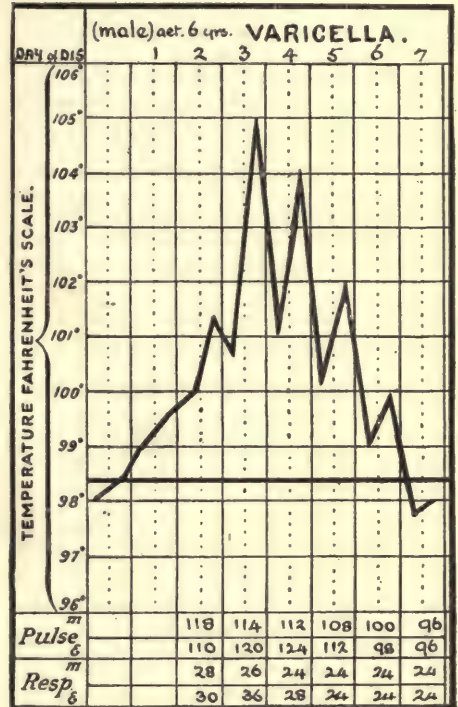


FIG. 27. A severe case of chicken-pox with high fever. Note the gradual ascent as the eruption develops.

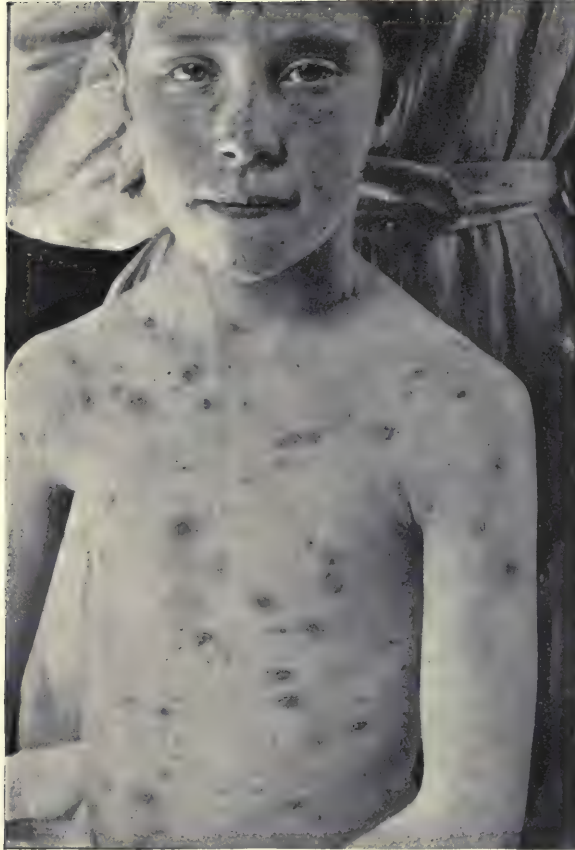
and general feelings of discomfort will also be present. In young children delirium is not infrequently seen. The child is restless and irritable, and, being often worried by the *itching* of the spots, makes his condition worse by much scratching.

Just as erythematous *rashes* occur in the prodromal period, so also rashes occasionally appear in the eruptive stage. It is reasonable to regard them as septic in character, the chances of infection from the skin being very considerable. Rolleston has pointed out that they are more liable to occur

in patients who have recently suffered from some eruptive fever such as scarlatina, the resistance of the skin having been diminished by the pre-existing eruption. This view is supported by the fact that such 'accidental rashes' are certainly not uncommon in varicella when it affects scarlatina convalescents. The rash is usually scarlatiniform. When it is very intense it may become purpuric, small hæmorrhages occurring as the result of rupture of the capillaries. I have, however, never seen an example of either a purpuric or a morbilliform rash, and cannot believe that these varieties are common.

SECOND ATTACKS of chicken-pox are very rare. I have never yet seen the disease in a patient who was believed to have suffered from it previously. On the other hand, some German writers have gone so far as to assert that second and even third attacks are comparatively common. We may say with confidence that this at least is certainly not the case. On the contrary, we might be justified in holding the view that of all the eruptive fevers chicken-pox is perhaps the least likely to occur twice in the same person.

COMPLICATIONS. There is little to be feared in the way of complications. It is very doubtful if most of the conditions which are described as occurring, such, for instance, as broncho-pneumonia, are not merely accidental. *Nephritis* is, however, worth mentioning. It has been reported by several writers, as a sequela of chicken-pox, and it may be directly due to the infection itself. I have only seen two such cases. One patient was sent into hospital on account of the nephritis, and had certainly varicella crusts on the body at the time. In type the nephritis resembled that seen in scarlatina, but whether its onset preceded or followed the attack of chicken-pox there was no satisfactory evidence. In another case the patient presented, together with typical vesicles, a scarlatiniform rash on admission, and, when the nephritis occurred thirteen days later, I assumed that she had really had the two diseases concurrently and sent her to a scarlet-fever ward. She showed no very definite desquamation and contracted scarlet fever. It is just possible that it may have been a relapse, but the circumstances pointed to the nephritis being due to chicken-pox. I have had no experience of the *laryngitis* which is said to occasionally complicate the acute stage of the eruption, but should the mucous membranes be much involved it is easy to see how inflammation of the glottis and subsequent obstruction might arise, just as it does in small-pox. *Eye complications* are in my own experience extremely uncommon. Rolleston has described a case of palpebral gangrene, and catarrhal conjunctivitis and keratitis are occasionally observed. As is the case with the other infectious diseases, nervous sequelæ have also been reported.



CHICKENPOX.

Showing ordinary distribution.

SEVERE TYPES. Two are usually described, the *hæmorrhagic* and the *gangrenous*. Of these the first is very rare, and it has not been my good fortune to see an example of it. The vesicles are said to be few in number. Hæmorrhages occur into the skin and into the base of the vesicles. Severe as the condition appears (there is even occasionally hæmatemesis), McCombie states that it is not usually fatal. The gangrenous type of the disease is by no means common, but may sometimes be seen in badly nourished and tubercular children. It is, as Goodall has stated, more the result of a septic infection of the pre-existing lesions than a real type of the original infection, although, as Knowles has pointed out, it may originate from the hæmorrhagic type of case, the blood-filled vesicles drying up into small black patches of gangrene. In the few cases which I have had the opportunity of observing the vesicles developed normally. A certain proportion of them, when the contents had become purulent, increased considerably in size and became surrounded by a marked inflammatory zone. Thick crusts formed, and from the necrosis of the subjacent and surrounding tissue gradually became larger, purulent material oozing from under their edges. The separation of the crusts left irregularly-shaped punched-out ulcers, with a sloughing base, sometimes nearly an inch in length. These in some cases increased in depth, the muscles being sometimes exposed. Such ulcers, indeed, have been described as eating their way down to the bone. Repair, if it takes place, is slow, and too often a fatal result ensues. The patient suffers from fever and wastes rapidly. In one or two of the cases, however, which I have seen terminate fatally, I have been at a loss whether to attribute the wasting and gradual loss of strength to the sloughing ulceration of the skin, or whether to assume that the enfeebled condition of the patient was responsible for the chicken-pox taking on this particularly severe type. All my cases were children barely convalescent from severe types of scarlatina, and their resistance to ordinary septic micro-organisms was probably much impaired. When the number of the ulcers is limited, recovery may be hoped for. Very ugly puckered depressed scars are left as the result. It may be noted that some authorities hold that many of the cases of so-called gangrenous varicella have in reality not suffered from chicken-pox at all. I have never seen an example of the rare type described as 'varicella bullosa', though pemphigus, which it apparently resembles, has complicated at least one of my cases.

DIAGNOSIS. Usually the diagnosis is easy, particularly if the patient is seen early. The rapid appearance of the clear vesicles, coming out in successive crops, and as a rule not preceded by any prodromal symptoms, leaves little room for difficulty. The really typical vesicle, with its tendency

to assume ovoid shapes, its delicate pellicle, and its almost transparent contents, is quite characteristic. Even in difficult cases one or two such vesicles can usually be found unbroken, and, once they are seen, the diagnosis is made, even if the eruption as a whole appears anomalous. It is also important to keep constantly in mind the characteristic distribution of varicella, as this assists us not only in distinguishing it from small-pox but also from various skin eruptions. It may be remarked that the flanks are usually well spotted, and the axilla is often invaded.

The differential diagnosis from *small-pox* has been considered at some length in the section on that disease, and it is unnecessary here to do more than recapitulate briefly the main points on which the distinction rests. And, firstly; it is well to remember that, in a patient of under ten years of age with a profuse eruption and good vaccination marks, the condition can hardly be anything else but varicella. During small-pox scares I am called to see many such cases, and have noticed that it is usually in patients who present a very profuse eruption that the difficulty arises. Believing firmly in the power of vaccination to modify the amount of the eruption, even if it cannot after a certain number of years prevent the disease, I have always been accustomed to lay great stress on the patient's age and his condition as regards vaccination in coming to a conclusion. The few well-vaccinated children of under ten years of age whom I have seen with small-pox have always had extremely scanty eruptions. The eruptions which alarm the practitioner during a small-pox scare seem always to be profuse ones.

A patient's history of illness, particularly in children, must not of course be relied upon too much. Still, those cases of chicken-pox in which prodromal symptoms have been noticed are usually severe and have a large number of skin lesions. The average case seldom suffers from initial symptoms. On the other hand, even the mildest of varioloids has a well-marked prodromal stage. A scanty eruption and severe initial fever would point, then, to small-pox.

The distribution of the eruption, the forearms suffering least, is of much importance. The appearance of the eruption in any given area of skin, all the stages of lesions being often represented and lying side by side, is hardly less so. In small-pox the face and forearms suffer most, and, except in varioloid, in which certain elements of the eruption often abort, all the lesions on a given area are approximately in the same stage. As regards the actual pocks themselves, the characteristic oval shape of many chicken-pox vesicles is not to be met with in small-pox eruptions. Even if a half-emptied vesicle presents 'false umbilication', its edges are usually irregular

and puckered, and its general appearance has only a remote resemblance to the small-pox pustule. It is as well not to lay much stress on the results of pricking a vesicle. I have seen the vesicles of a case of varioloid completely collapse, and, on the other hand, some varicella lesions do not empty completely when punctured. Chicken-pox is said to show either a normal blood count or a leucopenia, but I have on several occasions noted counts of from 20,000 to 24,000 leucocytes in children.

Chicken-pox may also be confused with certain *skin diseases*. Of these we may mention *impetigo*. This is in most cases chiefly distributed on the face, but occasionally the pustules or crusts are sufficiently numerous all over the body to cause difficulty. The presence of vesicles, or of their remains, in the mouth would be in favour of the eruption being varicella, as the mucous membranes are not affected in impetigo. After the crusts of chicken-pox have separated and re-formed once or twice, they are apt to resemble those of impetigo, and by this time it will be too late to expect to find somewhere on the body a typical vesicle, which at an earlier stage might have settled the question. In such circumstances we must depend on the distribution of the eruption. Such cases give difficulty occasionally in fever hospitals. A patient is admitted, with scarlatina or diphtheria, and the skin presents a number of crusts. Are these the remains of varicella? In doubtful cases it is safest to isolate.

I have recently had some difficulty on one or two occasions in distinguishing chicken-pox from *herpes*. As a rule the characteristic grouping of the vesicles of the latter allows of no doubt, but difficulties may occur. The question will be found fully discussed at the end of this chapter. I have had some trouble, also, with *dermatitis herpetiformis*, that is to say, the two cases of it which I have seen in hospital were so suspiciously like varicella that I thought it safer to isolate them in case of accidents. The vesicles in these cases had a strong resemblance to those of chicken-pox, and seemed to be as readily scratched open by the patient. The itching was also very well marked. The vesicles, however, continued to come out for a longer time than one would expect in chicken-pox, and there were no absolutely typical oval forms. Both children, moreover, had a history of several previous attacks, this skin disease being very apt to recur. I cannot help feeling that some of the second and third attacks of varicella which we read of were in reality instances of this disease. The vesicles, after drying up, left pale brown rings on the skin, and no definite scars.

Another skin eruption which may cause trouble is *pemphigus*, if in its early stages it only shows very small bullæ. Usually, however, large characteristic blebs appear and decide the nature of the case.

PROGNOSIS. This is always good in an uncomplicated case. If, however, the disease supervenes on an attack of some prolonged fever, such as scarlatina of the septic type, there is always a distinct possibility of the lesions becoming gangrenous. Should this happen, death may result, but how far from the chicken-pox and how far from the other condition it is not easy to say. Tubercular children also are liable to show the gangrenous form of the disease.

TREATMENT. Usually nothing need be done except keeping the patient in bed, which is always a wise precaution, even if the risk of nephritis need hardly be seriously considered. If the skin irritation is very severe, a dusting powder of boracic acid, zinc, and starch, in equal parts, may help to allay it. If a young child tears open the vesicles and scratches the sores it is a good plan to fix the arms in light poroplastic splints. In the crusting stage zinc ointment is a useful preparation. It aids the healing of the sores when the crusts become detached. When there is fever, the diet should be light and the condition of the bowels attended to. In afebrile cases a normal diet may be given. Should gangrene supervene, liberal feeding, iron and malt foods, and occasionally stimulants, will be useful. The ulcers must be treated on ordinary antiseptic lines.

PROPHYLAXIS. Although Thomson's experiments suggest that infection ceases after about nine days from the onset, it is wise, in the meantime, to isolate the patient until the last crust has separated. If I am certain that any given lesion has crusted over several times I relax this rule, removing the crust with a starch poultice and some blunt instrument, touching up the surface with some antiseptic, and disregarding any scab which may subsequently form. The quarantine for exposed persons should be at least three weeks. To secure perfect safety, twenty-five days would be better, but I have used the shorter period so far with almost complete success, incubations of a longer time being apparently very rare. I would permit any child to attend school for the first ten days of this quarantine period, this time, of course, to be calculated from the first exposure. Such a method would save a great deal of school time.

The relationship of chicken-pox and herpes. The interest recently taken in this question seems to make it advisable to add a note upon the point. Bokay in 1892 reported that he had seen nine cases in which chicken-pox appeared from eight to twenty days after an attack of herpes zoster had affected another person in the same family or hospital ward, and when the possibility of the chicken-pox having arisen from any other source could apparently be excluded. Of recent years numerous similar occurrences have been described by, amongst others, Heim, Orr, Milne, Richardson, and

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SEVERE CHICKENPOX.

Note the unusually profuse eruption on the hands and forearms. The individual lesions are typical of chickenpox, and are seen to be in different stages. The face has suffered comparatively little.

Cranston Low. A number of cases have been collected by Parkes Weber in an exhaustive paper on certain peculiarities of herpes zoster, and Le Feuvre, a firm believer in the identity of the two infections, has made an analysis of fifty cases illustrating their singular connexion. In forty-one of these chicken-pox followed herpes zoster within the limits of the usual incubation period, in five the shingles appeared in from two to five weeks after the chicken-pox, while in four the two conditions coexisted, typical chicken-pox developing in three or four days after the outbreak of herpes. We may supplement this by mentioning one of Cranston Low's observations, a case of two children in the same ward developing the one herpes zoster, the other chicken-pox within two days of each other. It must also be remembered that herpes is known to occur in epidemic form, and Heim notes one such outbreak as occurring together with an epidemic of chicken-pox in 1912 in Budapest.

Some years ago I should have been inclined to dismiss this subject as not worthy of serious discussion, and attributed many of the cases reported to coincidence. But the facts given above are sufficiently impressive to compel attention, and two recent cases of my own, which may be added to those in the third group of Le Feuvre, have at least emphasized the fact that there may be great difficulty in distinguishing the two conditions. The first, a small girl, developed what appeared to be an absolutely typical herpetic patch over the left shoulder-blade. Next day, however, a few outlying vesicles, one apparently typical of varicella, appeared in the neighbourhood of the patch, and one or two more on the right side of the back. There was nothing at any time below the waist line and nothing on the face, scalp, or limbs. I sent her to a chicken-pox ward, where she did not contract the disease, and seventeen days after the date of her removal one of the children exposed developed varicella. The second case, a few days after admission to hospital with diphtheria, developed a profuse herpetic eruption. The distribution on the first day was entirely limited to the area supplied by the posterior divisions of the spinal nerves, but was equally well marked on both sides. Next day there was one spot on the face and herpetic groups above both elbows, limited apparently to the supply of the upper division of the external cutaneous branch of the musculo-spiral nerve. On the succeeding days, however, other vesicles much more typical of chicken-pox appeared on the flanks, chest, and abdomen, and two other children in her own home were reported as having developed ordinary chicken-pox on the day of her attack.

These cases show at least that the varicella eruption may occasionally present a very interesting and curious distribution which may be limited

for the most part to the supply of particular nerves. Dr. Brownlee, formerly of the Glasgow Fever Hospitals, told me that he also has been impressed by this peculiarity. It will be noted that, in both the cases described, an original diagnosis of herpes had to be modified into one of chicken-pox a day or two later, and that they thus conform to the third group of the cases collected by Le Feuvre. There was in neither any form of irritation likely to influence the localization of the distribution and cause the eruption to come out early and cluster at any particular point. Hamburger has suggested that some instances of herpetic arrangement might be explained in this manner, and that badly-fitting corsets, for example, might determine the distribution of a chicken-pox eruption in such a way that it resembles a zona.

In the last eighteen months three out of seven appearances of herpes zoster in my wards have been followed by cases of chicken-pox, otherwise quite unexplained. I have also admitted a case of chicken-pox which in a similar way followed herpes at the Royal Hospital for Sick Children.

Cranston Low has made the interesting suggestion that an identical virus may act either through the nervous system or through the blood-stream, in the first case causing herpes affecting certain nerve endings and, in the second, ordinary chicken-pox. The mixed eruptions he would explain by a secondary infection of the blood from an original focus in the nervous system which possibly is invaded, as is the case in poliomyelitis, along the lymphatics round the olfactory nerve.

It is undoubtedly the fact that many adult patients suffering from herpes are able to give a definite history of chicken-pox in childhood, and this is to some extent an argument against the theory of identity. Nevertheless, enough has been stated to emphasize the importance of further investigation of this problem, investigation which can best be undertaken by the general practitioner, who, in addition to collecting cases illustrating the alleged relationship of these conditions, should particularly observe in what proportion of instances herpes, occurring in a household of children susceptible to chicken-pox, is actually followed by such infection. It might be well if some local authorities would imitate the example of the municipality of Bulawayo, which, no doubt at the instance of Dr. Le Feuvre, has made 'shingles' a notifiable disease. In the meantime we may leave the question an open one.

Those interested are advised to read the papers by Parkes Weber, *International Clinics*, vol. iii, series 26; by Le Feuvre, *British Journal of Dermatology*, 1917, p. 273; and by Cranston Low, *British Medical Journal*, Jan. 25, 1919.

CHAPTER VIII

TYPHUS FEVER

Introduction.

Etiology: geographical range: predisposing factors: infection and dissemination: bacteriology.

Period of Incubation.

Period of Invasion.

Period of Advance and Eruption: the temperature, the eruption, the odour, appearance and expression, circulation, respiration, urine, delirium, &c.

Stage of Defervescence: the crisis.

Stage of Convalescence.

Types of Typhus.

The Fever in Children.

Relapses and Second Attacks.

Morbid Anatomy.

Complications and Sequelæ.

Diagnosis: differential diagnosis.

Prognosis.

Treatment.

Prophylaxis.

Synonyms—Jail Fever, Camp Fever, Ship Fever, Brill's Disease, Tabardillo (Mexico). *French*, Typhus exanthématique. *German*, Fleckfieber.

INTRODUCTION. Typhus fever is now but rarely met with in this country, and, indeed, modern sanitation may fairly claim to have stamped it out: yet it was once so generally prevalent that Murchison has said that a complete history of typhus would be the history of Europe during the last three and a half centuries. The various names which have been given to it are most suggestive of its ravages in the prisons, armies, and fleets of the seventeenth and eighteenth centuries, and it was only towards the end of last century that it commenced to be effectively held in check. The experience of cities in which the disease was formerly endemic, such as Edinburgh, has been that the improvement of dwelling-houses, the opening up of congested areas, the destruction of slum property, and the compulsory notification of infectious diseases have made large epidemics impossible. In Edinburgh, during the ten years 1862 to 1871, no less than 2,824 cases of typhus were treated in the Royal Infirmary alone, and this number would represent only a small proportion of the actual cases occurring in the city. In the ten years after the introduction of the Notification Act in 1880 the total number of cases in the city was only 355, and in the succeeding ten years had fallen to 138. Considering that Edinburgh had for long enjoyed a most unenviable reputation for the prevalence of typhus, these results are very remarkable, and go far to show that, given a vigorous Public Health administration and an intelligent municipality, this disease, once so formidable, is at the present time of but little importance. In the old

days the students and resident physicians of the Edinburgh Royal Infirmary had a most practical acquaintance with the fever. A large proportion of them contracted it ; many died of it. To-day, on the other hand, the great majority pass through their course without seeing a solitary example of the disease. It is, indeed, only this want of experience on the part of the younger practitioners which makes possible the small outbreaks which are still occasionally liable to occur. The fever is common in Eastern Europe and from time to time is imported by immigrants. Only too frequently the first cases are missed, and as a result there is some spread of the infection. Typhus, then, rare as it is, is still worthy of study, especially by those who practice in large cities and in seaport towns.

But, apart from the necessity of some knowledge of this disease in the interests of public health, there are few acute fevers which are more interesting to watch. It is in fact the type *par excellence* of an acute toxæmia. The symptoms presented by enteric fever, rheumatic fever, or lobar pneumonia, when they assume that markedly toxic type known as the *typhoid state*, are the symptoms which are common to the vast majority of cases of typhus fever.

ETIOLOGY. Geographical Range. Typhus appears to be generally distributed all over the world. It has at different periods been common in most parts of Europe, and is still to-day prevalent in Russia and in the Balkan States. Its terrible ravages in Serbia during the war are fresh in the memory, and, introduced no doubt from Russia, it was responsible also for very many deaths in several of the German prison camps, the shocking sanitary conditions of which favoured its dissemination. Great Britain suffered much from it up to the middle of last century, and it persisted in Ireland and Scotland much later, occasional outbreaks being still observed in both countries, as, indeed, also in some of the great English seaports. Immigrants from Eastern Europe appear to have recently imported it to the United States, where, in an exceptionally mild form, it was for some time termed *Brill's disease* before it was identified. It is common along the whole North African coast, in Morocco, Algeria, Tunis, and Egypt. It has been also observed on the northern frontier of India and in Kashmir. It occurs sporadically in Eastern Asia, in Cochin China, Formosa, and China, and Musgrave and Stanley have recognized it in the Philippine Islands. Anderson and Goldberger have proved its identity with *tabardillo*, a fever common in Mexico. It may be added here that a very hot climate is unfavourable to the prevalence of typhus, as in Mexico it has been found that lice disappear when a person infested with them moves from a temperate to a tropical region.

Predisposing Factors. As regards the conditions which favour an outbreak it has long been recognized that typhus is a disease associated with dirt and destitution. The most important predisposing cause was considered to be *overcrowding*, with the massing of large numbers of persons together into an insufficient air space, and even with our present knowledge we may admit that unless such conditions exist large epidemics are impossible. *Season* has been found to be of some importance, as in winter, when windows are kept fast shut and the poor are driven into their houses instead of spending much of their time in the streets, the disease is more difficult to control. *Sex* exercises little influence. Males and females are affected, to all intents and purposes, equally. It is true there is a slight preponderance of males up to the age of twenty-five, and that afterwards females predominate. As regards *age*, it would appear that all ages are susceptible to the fever. Cases have been reported in patients as old as 92 and 104, and occasionally, though comparatively rarely, infants at the breast may be attacked. Perhaps the greatest number of cases will be found to occur between the ages of fifteen and twenty-five, though I believe that children contract the fever in a much higher proportion of cases than statistical tables show. I have found that when quarantine of the infected families is rigidly enforced the number of children suffering from the fever is very great, and, as the disease is not infrequently mild and abortive in the young, it is probable that cases in children are often missed unless the families are under that constant supervision which quarantine allows. It may be granted that after the age of twenty-five the chances of contracting the fever steadily diminish.

As with other acute infections, there is little doubt that exhaustion after a previous illness, fatigue, starvation, alcoholism, fear, anxiety, and worry may all lower the immunity of the individual sufficiently to increase his liability to take the fever. It is customary, then, to regard these conditions as predisposing causes.

Infection and Dissemination. To contract the fever it is necessary to be in almost absolute contact with an infected person. The 'striking distance' of the infection is extremely short, but our Edinburgh experience has been that to contract infection it is sufficient to enter the room occupied by the patient even if he is not actually handled or touched. We used to consider that the virus was readily destroyed by fresh air. An extremely short time of exposure to infection is probably all that is required to contract it. The comparatively close association with the patient which is necessary is well illustrated by some observations made by Harvey Littlejohn, who, during one of our last outbreaks, noted that even in large overcrowded

tenements, where several families occupied different rooms on the same flat, the fever did not spread from one family to another unless individuals were in the habit of entering each other's rooms. Those persons who were not on intimate terms with the infected families escaped, although their rooms opened on to the same narrow and imperfectly ventilated landing, and although they passed each other daily on the same staircase. This was certainly a strong argument against any form of aerial convection of the virus, and no doubt it was from the study of conditions such as these that some observers were, on purely epidemiological grounds, led to the conclusion that the fever was *disseminated by body vermin*, as has since been experimentally demonstrated by Nicolle and others. Thus in 1907 Professor Matthew Hay attributed the spread of the disease in Aberdeen to the agency of fleas, and in the following year Captain Hepper reported that he had controlled an outbreak of the fever in the Peshawur gaol by the systematic destruction of bed bugs. Captain Patton, moreover, in 1907 had remarked that a species of bug, common in Europe, is found in the North-West Frontier Province but not in other parts of India, and that its distribution curiously coincides with that of typhus.

In 1909 Nicolle, working in Tunis, reported the first successful inoculation of the disease in an anthropoid ape. This was confirmed by the researches of Anderson and Goldberger, who, working independently, had also proved the possibility of giving the inoculated disease to monkeys, and that it was in reality typhus. A successful inoculation, whether by intravenous, intraperitoneal, or subcutaneous injection manifests itself by a fever which appears after a varying quiescent period and commences and terminates abruptly. Animals which present such a reaction are immune to subsequent inoculations. The disease in monkeys is mild in character, but Anderson and Goldberger had a mortality of about 2 per cent. in their subjects. These observers concluded from experiments carried out by Nicolle and by themselves that 'satisfactory evidence has not yet been adduced that the blood of monkeys is virulent in the prefebrile stage, and that the blood may still be virulent twenty-four to thirty-two hours after the return of the temperature to normal'. Although it has been suggested that the virus lies in the white cells there seems evidence that it is extracellular, and facts seem to point against its filterability.

We owe to Nicolle, Comte, and Conseil the actual proof that *typhus* is *transmitted by the body louse*. This fact at once explained many of the peculiarities of the epidemiology of the disease, such as its association with dirt and overcrowding, and its short 'striking distance'. It was confirmed by the work of Ricketts and Wilder and also by Anderson and Goldberger. We

may add that in the opinion of the authorities quoted the flea and the bug play no part in the transmission of the fever. It is not improbable, however, that the *pediculus capitis* may be capable of conveying the virus.

As regards *fomites* it is clear that clothes, bedclothes, mattresses, and similar articles must be regarded as a source of danger. I have myself seen a small outbreak arise, in a provincial town in Scotland, which was satisfactorily traced to the sale of infected bedding. On one occasion also one of our sanitary officials contracted the fever from merely throwing typhus-infected fomites into a destructor with a pitchfork. Another official had previously removed them from the infected house, and the patient had had no other opportunity of contracting the infection. Another Edinburgh outbreak was possibly due to furs imported from Eastern Europe. It would seem reasonable, indeed, to regard as dangerous any articles which are capable of harbouring lice.

While we may consider that it has been proved beyond all doubt that the disease is normally transmitted by the louse, it is legitimate to speculate whether it is in any circumstances transmitted either by droplet infection or in any other manner. We used to believe the virus was inhaled, and the frequency of accelerated breathing and pulmonary symptoms gave colour to such a supposition. It may be recollected also that in the case of plague the causative micro-organism can either be inoculated or, in the pneumonic form of the infection, inhaled. In the present state of our knowledge, however, we will be well advised to regard the louse as the sole medium of transmission, and if, as has been suggested, any developmental changes of the infecting organism occur in the body of the louse, its agency would appear to be required to secure infection.

As to the *period of infectivity* clinical experience shows that a patient is infectious throughout the course of the fever, and that there appears to be some risk of communicating the disease also in convalescence. The duration of hospital isolation in Edinburgh has been five weeks from the onset. Our views on this point may have to be modified, but it must be remembered that, even when a convalescent is free from lice he may be discharged home to verminous surroundings with his blood perhaps still infective. Again, Nicolle states that a louse can transmit the infection to its offspring, and the persistence of nits may have to be considered. Experiments on animals will no doubt ultimately determine how long the infectivity of the blood persists; we have quoted above the opinion of Anderson and Goldberger. It may be noted, in conclusion, that a louse is not capable of transmitting infection earlier than four, or later than seven, days after a meal (Nicolle).

Bacteriology. The last statement suggests that some further phase

may have to take place in the life history of the unknown causative organism of typhus before infection is possible, and it is therefore not improbable that it may prove to be protozoal in nature. Numerous bacterial micro-organisms have been described, chiefly varying types of diplococci. Ricketts and Wilder discovered a short bacillus in the blood of patients and in the bodies of infected lice, but their work lacks confirmation. Plotz considers the disease is caused by a pleomorphic bacillus, but his attempts to cause typhus in animals by its means are far from convincing. Hort and Ingram recovered a very minute filter-passing organism from the blood, urine, and cerebrospinal fluid of typhus patients, and consider that some of the bacterial forms described by other observers may represent harmless phases in the life history of the causative germ. Prowazek found in the leucocytes certain deeply staining bodies,¹ which are possibly protozoa, and more recently Futaki has discovered a spirochæte in the kidneys and urine and also in lice. Wilson also has reported the presence of an organism in the blood, detected by the use of dark-ground illumination. He appears to be in doubt whether it is a bacillus or a spirochæte, but favours the latter view pending the further investigation which is so obviously required before the causation of typhus can be satisfactorily explained.

PERIOD OF INCUBATION. The length of the latent period seems to be very variable, from five to twenty-one days having been stated to be the limit. Authentic instances of shorter periods, two and four days, have been reported, however, by Murchison and by Curschmann, but such brief incubation stages must be extremely rare. In the case of one observer who inoculated himself with typhus blood the interval was eighteen days. In inoculated apes and monkeys the period was from four to twenty-eight days, usually in the latter animals from five to twelve, and in the former from five to eight days. No doubt the length of the stage is influenced by the date at which the infecting lice had their last meal, and also on the date on which the patient is first bitten by the invading vermin. It has been my good fortune to see only two cases in which the possibilities of exposure were absolutely limited to one particular hour, and in these the disease developed twelve and thirteen days afterwards. As regards the longest time which may elapse before the appearance of the first symptom, twenty-one days may be regarded as the extreme limit. Incubations over fourteen days must be very rare. In Edinburgh our quarantine period is a fortnight, and I have never seen any of the many persons who have undergone that period of

¹ These very minute bacillus-like bodies, known as *Rickettsia prowazeki*, are found in large numbers in lice four or five days after they have been fed on typhus patients. They do not appear to be found in normal lice, although this point has been disputed.

seclusion develop the fever after their release. But in the case of one child, who remained in quarantine because the other members of the family had all been removed to hospital, the first symptom occurred on the seventeenth day after the last possible exposure, so that occasionally the period of incubation must exceed that length of time. Nevertheless a fortnight may be regarded as a sufficient quarantine to exact for practical purposes.

PERIOD OF INVASION. The onset of typhus is very sudden, and it is usual for a patient to be able to tell, not only the day, but often the actual hour of his first symptom. This is, in most cases, *headache* of an exceedingly distressing character. Accompanying this is *chilliness*, which is nearly always well marked. The patient cannot keep warm, and is apt to sit in front of the fire and to wrap himself up with extra coverings. Slight shiverings, or actual rigors, may also occur. It has been said that, while *nausea* is frequent, *vomiting* is rare. This is not my experience. Almost all my younger patients vomited, and nearly half the adults also had this symptom. The three symptoms, headache, vomiting, and definite sensations of extreme chilliness, were found in combination in 37 per cent. of my cases. As the temperature commences to rise with the first complaint of the patient, the ordinary symptoms of fever and toxæmia, such as loss of appetite and insomnia, are also present. Convulsions may occur in children.

The mental acuteness of the patient is blunted from the first, and he usually shows more or less stupidity when asked questions. His *appearance*, even at this early stage, is often most suggestive. The face is usually congested, the expression is stupid, and the eyes are pink and sometimes watery. A sense of *prostration* is a prominent feature from the outset, and it is quite exceptional for the patient to keep on his feet after the third day.

By about the third or fourth day of the fever the *temperature* has reached its acme. But its rise to this level, often 104° to 105° F., is often very gradual. It is most exceptional in my experience to find a temperature as high as 103° on the first day of the illness. Our custom in Edinburgh, of isolating in quarantine all typhus contacts, has enabled me to watch many cases from the first symptom, and in only a few instances have I seen a high temperature on the first evening. Often the rise is only to 100° or 100·5°, and it is not at all uncommon to see a remission the following morning to nearly the normal line (Fig. 28). Some cases attain their maximum by steplike rises of temperature, as in enteric fever, but the rise is more rapid and, as a rule, to a higher level. During the stage of invasion the pulse is full and quick and the respirations are much increased in frequency.

STAGE OF ADVANCE AND ERUPTION. By the fourth day of high illness the patient may be said to have fairly entered on the continued stage

of his fever (Figs. 28, 29), and at about this time also the eruption is usually visible. In describing the symptoms presented by typhus from this stage onwards it will be convenient to commence with the characters presented by the temperature chart.

The course of the temperature. The main features of the fever are a continued high level, and little or no remission in the morning. I have many charts in my possession which show the temperature, taken every four

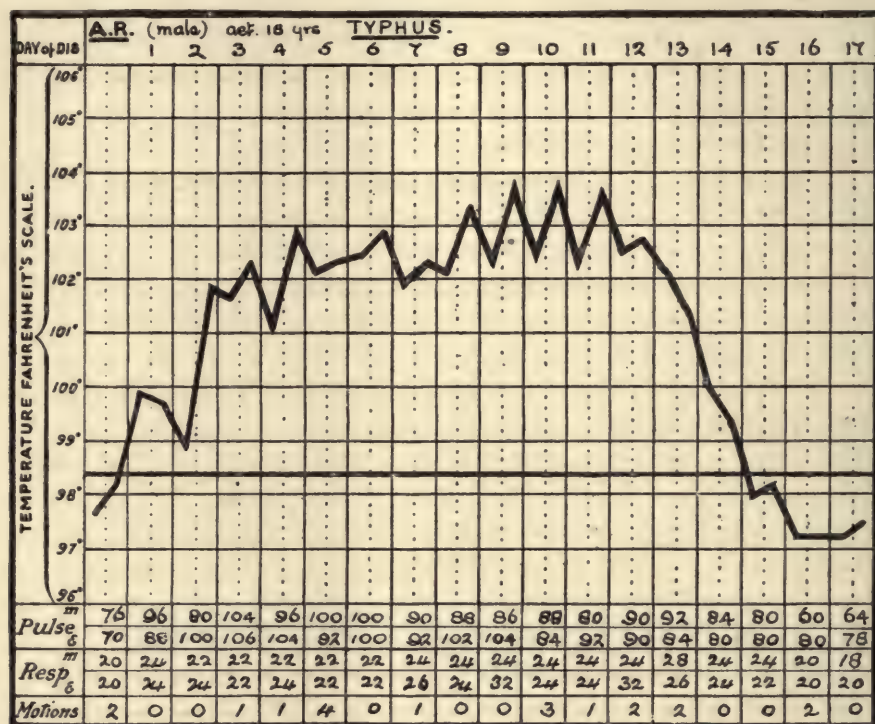


FIG. 28. A mild case of typhus with eruption well out from the fourth day. Note comparatively insidious onset. The good remission of temperature in the mornings of the second week and the low rate of pulse and respirations are favourable prognostic signs.

or sometimes even every two hours, running in a practically straight line and not varying more than two or three tenths of a degree. An average level would be from 103° to 104° F., but during the last few days of the first week this is not infrequently exceeded. An interesting peculiarity is the tendency to a *pseudocrisis*, which may occur any time between the seventh and eleventh days of the fever (see Fig. 31). The fall is sometimes considerable, but seldom lasting. As a rule the temperature rises again in a few hours, often to the same level as before, but perhaps more frequently to a point

somewhat below the previous figure. Although this attempt at a crisis is often wanting, there is usually some slight decline of the temperature from the seventh day onwards, and it is unusual for the fever in the second week to run quite so high as it does in the last days of the first. The true crisis usually commences somewhere about the thirteenth day and may be preceded by a slight rise in the temperature. But it may be delayed till as late as the seventeenth day, and I have seen it occur at any time between these two

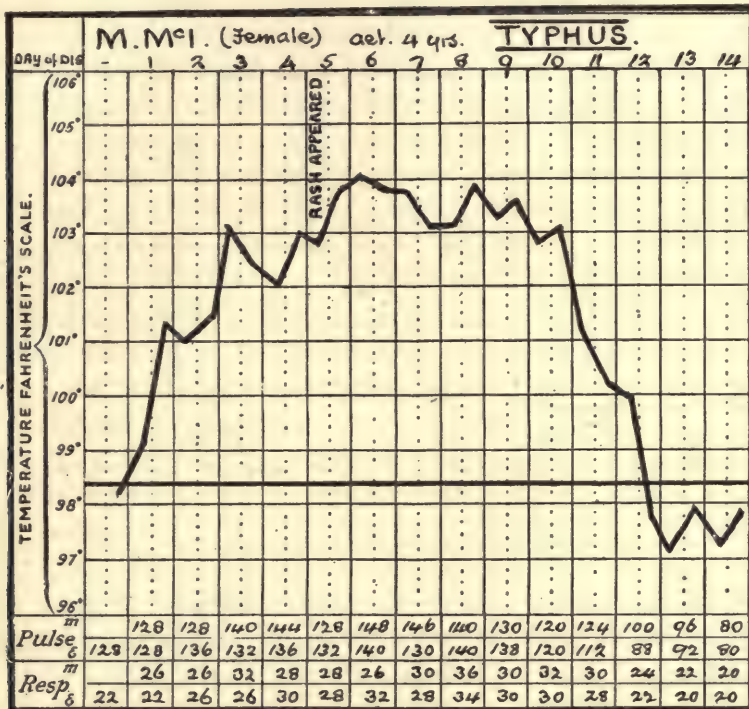


FIG. 29. Showing a sharp case of typhus in a child of four. Note the comparatively short duration.

dates. Should death be imminent the temperature nearly always rises and may attain hyperpyretic levels (see Fig. 30).

The eruption. The rash of typhus is usually well out by the fourth day. It may be said to consist of three main elements. First, *spots* appear upon the surface of the skin. In appearance they resemble very closely those of enteric fever. They are rose-pink in colour, and for the first few hours of their existence are distinctly raised above the skin and fade easily on pressure. Afterwards, however, they lose their raised character, and within a couple of days become a dirty brown colour and cease to disappear on pressure. As

regards distribution, this rash is present all over the body except the face, but is usually most profuse on the trunk, particularly on the back. The spots are somewhat irregular in outline and give a measly appearance to the skin of the patient. The second element of the eruption consists of similar spots, lying, not on the skin, but faintly seen as it were beneath it, and causing that marbled appearance which is known as *subcuticular mottling*. This is well seen on the trunk, and perhaps best of all in the axillæ, and may be best appreciated in a shaded light. Lastly, true hæmorrhage may occur either into existing spots, or independently of them, giving rise to dark purple *petechiæ*, exceedingly like vermin-bites, but lacking the central scar. All these elements, taken together, form what has been described by Jenner as the 'mulberry' rash of typhus.

The subcuticular element of the rash is often recognizable before the fourth day. In one instance I have found it present on the second, and it is quite commonly seen on the third. At this early stage the spots seem to be struggling to come definitely out on the skin, and by the fourth day they may, as has been said above, be raised above it. The spots and the mottling occur to a greater or less extent in practically all cases of the fever, but in mild cases often have to be looked for, the whole rash being extremely scanty and ill-defined. In children it may occasionally be wanting altogether. The petechial element is not nearly so constant, true purpuric hæmorrhages occurring as a rule only in patients who are sharply ill. Broadly speaking, the amount of the eruption, and its tendency to become hæmorrhagic in character, are in direct proportion to the severity of the case. Unless the petechial element is very well marked the rash begins to fade by degrees from the commencement of the second week of the fever, but staining often persists for several days after the crisis.

The odour. Typhus patients unquestionably throw off an exceedingly unpleasant odour which is distinctive of the disease. It has been compared to the smell of rotten straw, to that of mice, and by Hort to that of a wet umbrella beginning to dry. I think, personally, as did Murchison, that it is peculiar and unpleasant enough to be acknowledged as an odour *sui generis*. It appears to be given off from the skin of nearly all typhus patients at some period or other of their illness, and I have noticed it even late in convalescence. Its development is, I am certain, entirely independent of the condition of the patient as regards cleanliness, as I have found it well marked in patients who have been more than three weeks in hospital, and who have been sponged or bathed regularly at frequent intervals during that time. It is of undoubted value in diagnosis, and is possibly even better appreciated in the airy wards of to-day than it was when patients were often crowded

together with insufficient air space, and when imperfect nursing arrangements allowed all sorts of other odours to enter into competition with it.

Appearance and expression. By the commencement of the period of advance the appearance of the patient is usually thoroughly characteristic. The features are bloated and slightly swollen, the skin congested, and the expression is that of a drunken man. The conjunctivæ are injected, giving a red or pink colour to the eye, and the pupils are, as a rule, markedly contracted. It is remarkable to notice how quickly the features of a person of education and refinement can approximate in appearance to those of a drink-sodden dweller in the slums.

The circulation. In the early stage of the fever the *pulse* is merely increased in frequency, its rapidity being usually in direct proportion to the elevation of the temperature. As a rule it runs rather over than under 100. In the second week, as the heart commences to suffer from the prolonged toxæmia, its frequency is increased, it becomes small, and low tension and dirotism may be well marked. Irregularity may also be noticed in the last days of the fever, and in very rare instances the pulse may become extremely slow, rates of forty and even thirty per minute having been reported. On auscultation, it is found that the first sound early becomes faint or inaudible, and a diminution in the force of the cardiac impulse is perceptible.

The respiration. This is nearly always rapid, giving rise frequently to the idea that the real cause of the fever lies in the lungs. It is usual for the respirations to exceed thirty per minute, and in the second week forty is no unusual figure (see Figs. 30, 31). The great helplessness of the patient, and the severity of the toxæmia, often lead to marked hypostatic congestion of the lungs. This, indeed, appears so frequently that it may be fairly described as a symptom of the disease. Some degree of cyanosis is often present, especially in the later stages of the fever. A little bronchial catarrh is noticed in most cases, as in enteric fever, and many patients suffer from cough.

Alimentary system. The *tongue*, which from the first has been somewhat sticky and covered with a close white fur, becomes dry and brown in the centre by the time the temperature has reached its acme. Thereafter, if not carefully attended to, it is apt to get cracked and fissured, and covered with black crusts. In severe cases it is shrivelled and pointed, and in its shape and dark colour resembles the tongue of a parrot. The lips and teeth early become covered with sordes, and, if not cleaned regularly, the whole mouth is filthy. *Thirst* is a prominent symptom from the first, but, as the patient loses his consciousness, it is less complained of. The appetite is entirely lost. *Constipation* is the rule for the first ten days of the fever, but

some looseness of the bowels may be noticed in the later stages. Vomiting is not a very frequent symptom in the course of the disease.

The urine. The amount of the urine is reduced, its colour is dark, and its specific gravity much increased. During the first week the excretion of urea is excessive. Later on it may be diminished, and uræmia has been occasionally observed. Chlorides are diminished in quantity and may be altogether absent. *Albuminuria* is the rule in adult cases, that is to say, it was present in four-fifths of my cases during the whole febrile period. In children it does not occur nearly so frequently. The diazo reaction is, in my experience, invariably present in the stage of advance, and is, indeed, unusually brilliant in this fever.

The nervous system. It has already been seen that *headache* is one of the most constant symptoms of the invasion stage. It persists well on into the fever until the unconsciousness or apathy of the patient causes complaint of it to cease. It is usually frontal, but may in some cases be occipital or temporal. *Giddiness* is also frequently present, and pains in the back and limbs are commonly complained of. The intelligence is blunted and there is much mental confusion and loss of memory. *Deafness* to a greater or less degree is invariably noted. The patient may be apathetic and drowsy by day and is often wakeful and restless at night. In most cases there is more or less *delirium*. Should this occur during the first week it may be of the type of delirium tremens, and occasionally, if the patient is alcoholic, delirium ferox sets in. This is the wild maniacal form of delirium which is so dangerous both to the patient and his nurses. He struggles to get out of bed, fights with the attendants, and is capable of throwing himself from a window. One of my patients before admission required four strong policemen to restrain him. Another attempted to drink the oil from the glass reservoir of a lighted paraffin lamp which he actually broke with his teeth, cutting his mouth and burning his moustache. The strength of men, even of poor physique, when suffering from this form of mania is little short of marvellous.

By the beginning of the second week, however, the patient is usually too exhausted for such a form of delirium to be possible. This is the time for the low muttering type. The patient has entered the stage which has given the name to the 'typhoid state'. Too prostrated by toxæmia to do anything for himself, he lies helplessly on his back, sometimes picking aimlessly at the bedclothes, sometimes immobile in a condition approaching coma, with pin-point pupils and eyes fixed on the ceiling. The thorough poisoning of his nervous system is further evidenced by *subsultus* of the tendons, and by loss of control of the bladder and bowel reflexes. The urine is passed under him, or frequently he is so insensible to the calls of nature that no

attempt is made to pass it until too late, and *retention of urine* results. He no longer calls for water; it has to be forced upon him. Occasionally convulsive *twitching* of the muscles of the face, or less frequently of the arms, may appear towards the end of the second week. Tremor is also noticed in bad cases.

Summary of the stage of advance. The patient, then, suffering from many or all of the above symptoms, presents as perfect a picture of profound toxæmia as can be found in clinical medicine. From the moment his temperature has reached the height, and his rash has appeared, he is seriously ill and much prostrated. Till the seventh or eighth day of his fever his pulse may be good and his strength in delirium extraordinary. The delirium is intense in proportion to the amount of insomnia from which he suffers, and is most troublesome in alcoholics. With the beginning of the second week the strength commences to fail. The patient can no longer turn himself in bed, and the eruption is most profuse, especially upon the back. The respirations and pulse increase in frequency, although by this time it is not unusual for the temperature to decrease. The face becomes less congested, but more cyanotic in tinge, the pupils are smaller, and the ataxic symptoms more marked. In such a condition, passing all his excreta into the bed, and muttering incoherently to himself, he drifts through the few remaining days of his fever, often presenting such a hopeless appearance that it would seem impossible for him to recover. Should death supervene, a rise of temperature, often quite sudden and unexpected, occurs about the twelfth, thirteenth, or fourteenth days, the symptoms are aggravated, the respirations and pulse rise rapidly in frequency, and the patient succumbs within a few hours of the change being noticed (see Fig. 30).

STAGE OF DEFERVESCENCE. The great majority of patients, however, fortunately progress to a favourable termination. The *crisis* usually commences on the thirteenth day, but may be delayed till later. An evening fall of two degrees or thereabouts is often the first sign of it (Fig. 28). In other patients it may occur in the early hours of the morning, and the fall at that time of the day is apt to be greater. The crisis is not a rapid one, usually requiring two or three days to be complete (see Figs. 28, 29, 31), but, even if it seems a little prolonged, there is no doubt whatever of the critical nature of the change. It may, in some cases, be broken by a considerable evening rise of temperature, giving an appearance on the chart of a descent in two distinct steps. There is, in favourable cases, no heavy sweating, but the skin becomes comfortably moist. Occasionally a little looseness of the bowels, the so-called 'critical evacuation', may precede or accompany the fall of the temperature. The mental condition of the

patient rapidly improves as the pyrexia relaxes, and by the time the normal line is reached the appetite has often returned. Occasionally, however, death occurs just after the crisis from exhaustion or from the persistence of definite complications.

In some patients, usually children or young adults, the defervescence of the fever is by a rapid but distinct lysis, with well-marked evening swings of temperature, the normal being attained in some four or five days (Fig. 32).

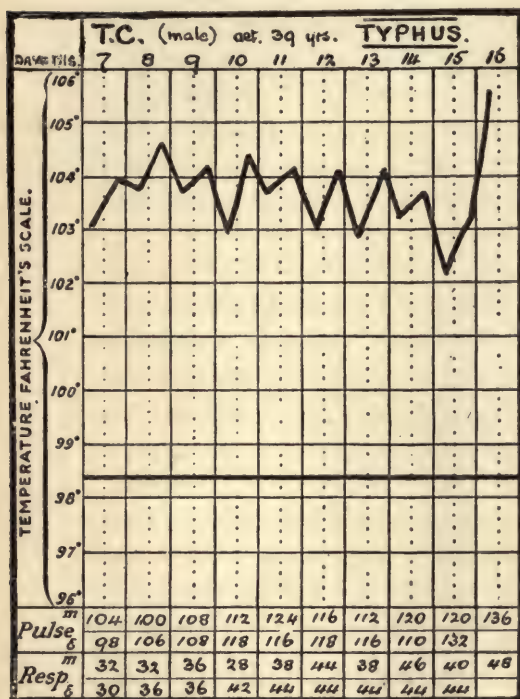


FIG. 30. A fatal case of typhus. Note the rapid respirations and the rise of temperature before death. Also that there is no marked decline of temperature during the second week.

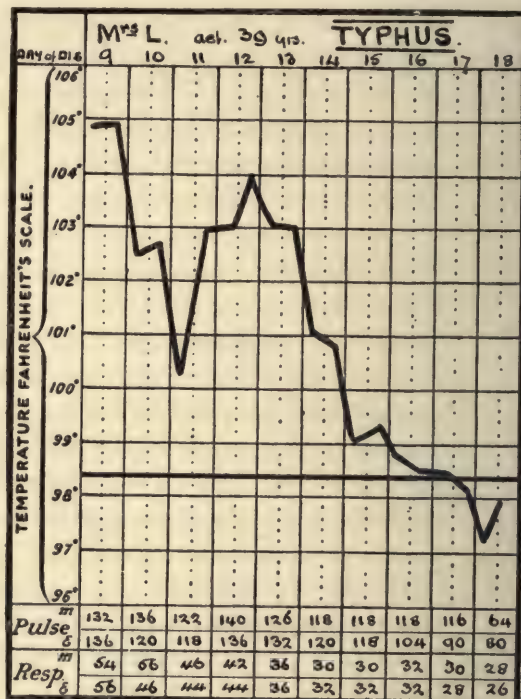


FIG. 31. A very severe case of typhus from the ninth day, showing a pseudocrisis on the tenth and eleventh days, and the true crisis on the fourteenth. Note rapidity of pulse and respirations.

STAGE OF CONVALESCENCE. The convalescence of typhus is usually uneventful and rapid. The temperature is apt to remain subnormal for several days. The patient, who has invariably been much emaciated by the fever, has a most hearty appetite, and regains both strength and weight with astonishing rapidity. It is not unusual for an adult to gain from a pound to a pound and a half daily. It is remarkable to see a patient, who less than a week previously was absolutely helpless and seemed most unlikely to recover, sitting up in bed and enjoying a liberal dinner of solid food.

A week after the crisis the average patient is quite willing to get out of bed, and is apparently perfectly able to do so. Many patients have no recollection of their fever at all. Others, however, carry with them for life a vivid memory of the hallucinations which haunted them in their delirium.

TYPES OF THE FEVER. The most common type of typhus, and that described above, is known as the ataxo-adyynamic form of the disease; that

is to say, it presents both marked nervous symptoms and great physical prostration. Occasionally, however, cases occur in which either the nervous or the asthenic symptoms definitely predominate, and these have been described as belonging to the ataxic and adynamic types respectively. Of severe forms the most remarkable is *Typhus Siderans*, or 'blasting typhus', a type which is fatal in two or three days from the onset, and which must closely resemble the fulminant form of cerebro-spinal fever. *Mild types* of the disease are much more common. Patients may occasionally pass through their whole fever without losing consciousness, with no nervous symptoms, and with no suggestion of cardiac weakness. The rash, again, may

be scanty, and occasionally only the subcuticular element is visible. Such slight cases of the disease may, however, present considerable pyrexia. The crisis often occurs early.

THE FEVER IN CHILDREN. As a general rule the fever, as it occurs in children, is of the mild type. Rashes are usually scanty and, while there may be considerable pyrexia and delirium, the worst features of the disease are not much in evidence. Even in severe cases, which are sometimes seen, the fever for the most part runs a short course and the crisis may occur as

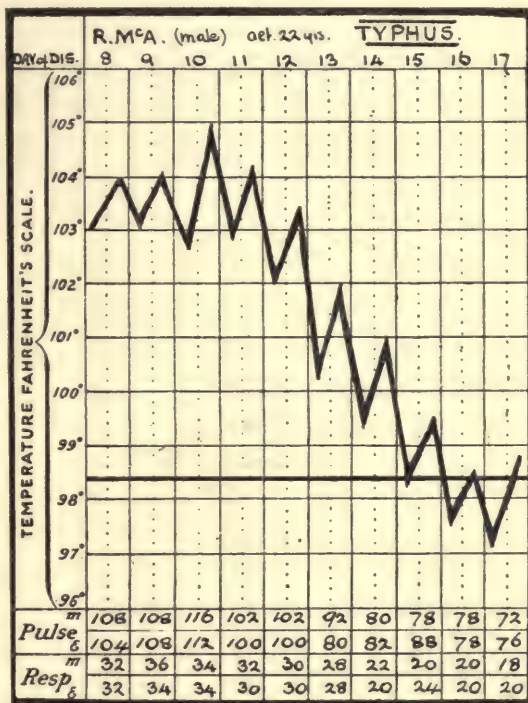


FIG. 32. Illustrating a somewhat unusual termination by a typical lysis in an adult. It will be noticed, however, that a very marked improvement in the pulse and respiration rates took place about the fourteenth day.

early as the seventh day, and is seldom delayed to the thirteenth (see Fig. 29). I believe that some children take the fever so slightly that it may be missed altogether; headache, sickness, and malaise being the only obvious symptoms, unless the temperature is taken. While termination by crisis is the rule, lysis occurs with comparatively greater frequency in the young.

RELAPSES AND SECOND ATTACKS. Relapse appears to be almost unknown. Murchison, with all his vast experience, never saw an instance of it, and quotes only one case, of Buchanan's, as a proof that it occasionally occurs. Second attacks, though more frequent, are also extremely uncommon. Murchison, however, had the fever twice himself, each time with well-marked symptoms, and a fair number of similar cases are on record. I have myself seen a woman in two attacks of the fever, the second occurring six years after the first. An interesting feature of this case was that, on the second occasion, the patient walked up to hospital on the second or third day of her illness and insisted upon being taken in, as she recognized the symptoms. Needless to say I was frankly incredulous, but a day or two later the course of the fever and the appearance of the eruption proved her to be perfectly right.

MORBID ANATOMY. Typhus cannot be said to have any characteristic post-mortem appearance. Decomposition sets in early and the autopsy should be made as soon as possible. All the internal organs are, as a rule, congested, and sometimes small hæmorrhages may be seen on their surfaces. The heart's substance is soft and friable, and its cavities somewhat dilated. The myocardium presents the characters of an acute parenchymatous degeneration. The lungs show great hypostatic congestion, often with consolidation at the bases. The spleen is enlarged, very soft, and occasionally diffuent. The membranes of the brain are congested and the lateral ventricles often distended with fluid. The intestine shows no ulceration. Attention has been recently directed to the so-called *typhus nodules* which can be detected by histological examination in almost all the organs of the body and, according to Jaffé, especially in the brain in the neighbourhood of the aqueduct of Sylvius. In this situation they consist of a spherical or fusiform dilatation of the small vessels, primarily due to damage to the intima and subsequently to a proliferative process in the vessel walls and the glia cells. The frequency of these lesions throughout the nervous system is said to account for the nervous symptoms of the fever. It is suggested that we have here a pathognomonic sign by which the disease can be recognized after death. Otherwise the presence of genuine petechiæ on the skin, together with the other appearances detailed above, would afford a presumption that a case was one of typhus.

The Blood in Typhus. Wilson, who has made a study of this question himself, and who has also summarized the literature, states that there is generally a leucocytosis. The polymorphonuclear cells are increased, but the most striking feature is the increase of large mononuclears and the absence of eosinophiles. A post-febrile eosinophilia is sometimes observed.

COMPLICATIONS AND SEQUELÆ. Broadly speaking, few acute diseases are so free from complications as is typhus, and the same may be stated as regards sequelæ. After the crisis, indeed, it is most unusual for a case to give trouble. During the fever, however, respiratory complications may cause anxiety, particularly *bronchitis*. If this is widely spread, and is accompanied by much secretion, the patient has, in his enfeebled condition and with his dorsal decubitus, little chance of adequately clearing his tubes, and, as hypostatic congestion is almost always present, death may occur by a slow process of suffocation, either before or just after the crisis. *Laryngitis* is a much less common but an even more dangerous complication, ulceration and necrosis of the cartilages being produced, or death supervening as the result of œdema glottidis. True lobar pneumonia is also rare, but I have seen two cases in which it undoubtedly occurred. Probably few severe cases escape a certain amount of *myocarditis*, which, indeed, might justly be regarded rather as a symptom than as a complication. *Venous thrombosis* is comparatively common in some outbreaks, and affects most frequently the veins of the left lower extremity as in enteric fever. Obliterative arteritis appears to be responsible for the *gangrene* which occasionally occurs and which seems to have been common in Serbia. Chesney states that much of the gangrene of the feet must have been due to the habit of Serbian patients covering their heads with their blankets and leaving their feet exposed. The condition was not so frequent in properly nursed cases.

In some patients *diarrhœa* may be sufficiently severe to assume the importance of a complication. It is exceedingly difficult to check, and is quite sufficient to turn the scale against recovery. Hæmorrhage from the bowel has been noted in rare instances, and would appear to depend more upon some general condition of the blood than upon any local lesion.

Occasionally the presence of tube casts and traces of blood in the urine suggest the presence of a true *nephritis*. I have seen one instance of acute nephritis occurring as a sequela in early convalescence. It appears, however, to be rare. Otitis media, boils, and small superficial abscesses are also occasionally seen in badly nourished persons after the crisis. Meningitis is uncommon, but hemiplegia, neuritis, and functional disturbances of the *nervous system* have been met with both during and after the fever. Some mental weakness, or actual mania, may occur as a sequela of typhus, but,

fortunately, according to Murchison such conditions seldom last more than two or three months. I have noticed very curious mental changes, as apart from any dementia, following the fever, and am inclined to believe that the mental attitude of a patient may be altered permanently.

A not uncommon complication is *parotitis*. There is good reason to believe that its frequency may be much reduced by careful nursing and attention to the cleanliness of the mouth. The fact that it has been extremely common in Eastern Europe points to this supposition. But I have seen it occur in patients who were certainly efficiently nursed, either shortly before the crisis or early in convalescence. Bubonic swellings of other glands have also been reported in typhus and suggest a relationship to plague.

While good nursing will do much to prevent them, large sloughing *bed-sores*, usually over the sacrum, will sometimes occur in spite of all precautions.

DIAGNOSIS. During the existence of an epidemic this is not, as a rule, very difficult. When, however, there is no typhus in the neighbourhood, a first case may give considerable trouble, if not well marked. In children also, even when there is a definite history of exposure, it may be difficult to come to a conclusion.

A sudden onset and early prostration should, if there is an outbreak, suggest the fever. The congested face, 'drunken' expression, and pink eyes are also very suggestive. So, too, are mental confusion and deafness. The importance of a history of headache, chilliness, and vomiting has been already insisted on. The presence of the rash, if it is well developed, is, of course, final, but unfortunately it is occasionally absent altogether, especially in children, or may consist merely of the faint subcuticular mottling which it requires a little practice to recognize. Moreover, the homes of the typhus patients are usually dark, and, again, the patients themselves may require a good wash before the rash can be seen. In doubtful cases it should be looked for in the axillæ and the groins, and it is best seen in the shadow of the raised bedclothes, being often imperceptible in a strong light. Dr. Murray, who has seen much typhus in the Hebrides, informs me he lays stress on the persistence of a pink spotting on the backs of the wrists, even after the rash has become indistinct elsewhere. I have had as yet no opportunity of verifying this interesting observation. Vermin bites may cause difficulty, but may be distinguished from typhus petechiæ by their well-defined outline, as well as by the minute puncture in their centre. To those who have had previous experience of the fever its characteristic odour, if present, will be of great assistance. It is best appreciated at the moment the bedclothes are first lifted to obtain a view of the rash. I have on several occasions diagnosed

typhus by it in patients sent into hospital as enteric fever, and who had at the moment no other definite typhus symptoms.

The principal diseases which may be confused with typhus may be with advantage considered in detail. *Lobar pneumonia* not infrequently causes some difficulty. Firstly, a case of pneumonia, usually apical, and accompanied by marked head symptoms, is not at all unlikely to be mistaken for typhus. Secondly, a real case of the fever may be regarded as pneumonia, the disturbance of the respiration, the cyanosis, and the dullness at the bases of the lungs lending colour to this view. In typhus, however, the dullness is not restricted by the limits of the lobe, there is no tubular breathing, and both sides are usually equally affected, the condition being a hypostatic one. In the absence of a rash, however, it would be safe to assume that a case which presented dullness at the apex was one of pneumonia only. The respirations in typhus, except in severe cases, which may be confidently expected to show a rash, are usually hardly so rapid as would be natural in a bad case of pneumonia. It is well not to be misled by herpes, as this condition has been reported as occurring frequently in some typhus epidemics. It cannot, nevertheless, be regarded as a common complication of the fever. It must also be recollected that lobar pneumonia may occasionally complicate the course of typhus.

The absence of a rash is the chief distinction of cases of *meningitis*. Again, in meningitis the senses are at first preternaturally acute, whereas in typhus they are dulled. The typhus patient, therefore, is not nearly so irritable, nor is he so liable to utter the cerebral cry so characteristic of children with meningitis. On the other hand, it must be admitted that meningism often occurs in typhus, and that squint, ptosis, inequality of the pupils, and the like, though more frequent in meningitis, have all been noticed in uncomplicated cases of the fever. From a recent experience of *cerebro-spinal meningitis* I should be inclined to think that the differential diagnosis might occasionally be difficult. There is often little or no head retraction in the early days of cerebro-spinal fever, and petechiæ are frequently seen on the skin. But these skin hæmorrhages are few in number, widely scattered, and there is no subjacent rash. In any case lumbar puncture would clear up a doubtful case at once.

Uræmia has frequently been confused with typhus, especially when supervening suddenly in a chronic kidney condition. The absence of rash and pyrexia should settle the question, the latter point being perhaps the most important distinction. Still it is always possible that a case of uræmia may present a temperature which may be due to some local inflammation. There should not be much difficulty in distinguishing the rash of typhus

from *purpura*. Here, again, the usual absence of pyrexia in the latter condition is a point of importance, and in *purpura* the hæmorrhages are commonly larger than in typhus, and there is no subjacent rash. The occurrence of hæmorrhage from the mucous membranes would favour a diagnosis of *purpura*, although, as has been seen above, such an event is not unknown in severe forms of typhus.

A fading *measles* eruption often very closely resembles that of typhus. A history of catarrh and of a well-marked rash on the face, which may often be obtained from the relatives of the patient, decides the diagnosis at once. The typhus rash does not invade the face to any marked extent, though it occasionally appears over the angles of the jaws. When the measles rash is well out on the body, and has not begun to fade, there should be no difficulty in distinguishing the two infections, the spots being more raised and larger than in typhus, of a much brighter colour, and more likely to assume crescentic arrangements.

As regards other diseases, I have seen mild cases of typhus treated as ordinary epidemic *influenza*. The distinction here is very difficult, unless the rash is sufficient to attract attention. Two cases have also come under my observation in which pain in the joints was so prominent a symptom that a diagnosis of rheumatic fever had been made.

The chief difficulty, however, which is likely to arise in the diagnosis of typhus fever is the distinction of the disease from *typhoid*. When we recall how comparatively recently the two fevers were finally differentiated, this is natural enough. A mild case of typhus, with little or no rash, very closely resembles enteric fever in appearance and symptoms. A severe case of typhoid, on the other hand, with a copious eruption of spots, which do not disappear well on pressure, may easily be mistaken for typhus. In coming to a diagnosis, the chief points to be noted are, firstly, the history of the case, a very definitely sudden onset being much against typhoid; secondly, the appearance and expression, which in typhoid is usually more refined and less 'drunken'; thirdly, the pupils, which are often dilated in typhoid, whereas in typhus they are usually contracted; fourthly, the conjunctivæ, which are clear in the vast majority of typhoid cases; fifthly, the temperature, which in typhus fails to show the tendency to morning remission so characteristic of typhoid; and lastly, the absence of true skin hæmorrhages and subcuticular mottling in typhoid, even when its spots are numerous enough, and deeply stained enough, to suggest the typhus eruption.

Unfortunately few of these points of distinction can be relied upon with much confidence. It is well known that on rare occasions a typhoid

fever may start with marked abruptness. A history, however, of very severe headache associated with vomiting and chills would be suggestive of typhus. Epistaxis may occur in the early stages of both fevers, but in my experience it is very rare in typhus, and its occurrence would somewhat prejudice me against a diagnosis of that disease. The severe cases of typhoid which are most likely to cause confusion may have, and not infrequently do have, small pupils and injected conjunctivæ. Moreover, their temperature tends to lose its natural morning remission, and to run in a comparatively straight line. I am inclined to believe, however, that, before these features are in evidence in a typhoid case, it may be assumed that the fever has lasted nearly a fortnight at the very least. A history of a longer illness would of course be very much against a diagnosis of typhus, which terminates in the vast majority of patients about the fourteenth day. At all events the occurrence of a crisis, or its failure to appear about that time, will settle the question within a day or two of the difficulty arising. The spleen is enlarged in both fevers, and its examination, therefore, gives us no help. The abdomen may be tumid in typhus and the stools may assume an enteric character if the patient has been carelessly dieted, so little assistance can be expected from the inspection of either.

As regards the *Widal test*, which, in the first edition of this book, I too confidently asserted could be relied upon to make the distinction, it must be regarded as of very questionable value. So far as my own experience goes, it is true that I only found it positive in two out of nearly a hundred cases of typhus, and I was inclined to assume that in the cases reported as positive by other observers the patients must have suffered previously from enteric fever. But Wilson found that eighteen out of thirty-one specimens of typhus blood examined in Belfast gave a positive agglutination test to the bacillus typhosus in 1-50 dilution, and is confident that the great majority of the patients concerned had not had a previous attack of enteric fever. During the Balkan War, moreover, Mr. Haigh wrote me that the Bulgarian physicians were classing many obvious cases of typhus as 'typhoid' on the strength of positive Widal reactions. This peculiarity of typhus blood is, according to Dr. Wilson, due to the presence in it of heterologous agglutinins. It is an interesting fact that Calmette has noted in typhus serum agglutinins capable of acting upon the *micrococcus melitensis*. Markl, studying a small outbreak in Trieste, failed to confirm this finding, and this taken together with my Edinburgh experience with the typhoid bacillus, and at that time I was working with as low a dilution as 1-30, shows that these heterologous agglutinins are by no means always active. But it must be frankly admitted that the value of the serum reaction in differentiating these particular fevers

is practically nil. The diazo reaction is unfortunately also valueless, as it is present in all cases of typhus.

The so-called *Weil-Felix reaction* has recently attracted attention. These workers recovered from the urine of typhus cases a short Gram-negative bacillus of *proteus* type, which they regard as a secondary invader and not the cause of the fever. This bacillus, called *Proteus X 19*, is agglutinated in high dilutions by typhus blood with such regularity that the test has been regarded by some German authorities as absolutely specific. It is not agglutinated by typhoid or normal serums. From a practical point of view the difficulty in applying the test would be the necessity of securing a culture of this organism, which does not appear to be present in many typhus urines, but has been recovered from the blood by Zeiss in 18 out of 301 patients.

PROGNOSIS. When we consider the chances of recovery of a patient suffering from typhus, we are most of all influenced by the question of *age*. In the first five years of life the mortality is, according to the tables of Murchison, for London, and Brownlee, for Glasgow, somewhere between 5 and 6 per cent. In the succeeding five years it declines, and in the third five years of life reaches its lowest point, about 2 per cent. Thereafter it steadily rises, reaching 30 per cent. between the ages of thirty-five and forty years, and being probably 80 per cent. in persons of over seventy years of age. In the last series of 151 cases which have been under my own observation the death-rate in persons of under twenty years of age was only 1.53 per cent.; between twenty and forty years of age it was 12.06 per cent., and in persons above forty years no less than 32.14 per cent. These figures, although referring to a very small number of cases, nevertheless give an adequate idea of how markedly the prognosis is affected by age.

As regards *sex*, females are admitted by most authorities to have a lower death-rate than males. In some outbreaks the comparatively small mortality rate of females is remarkable. My own cases show a percentage mortality of 6.7 for females as against 16.4 for males, but this difference is excessive and should not be depended upon. Taking merely the patients of over twenty years of age, only 10 per cent. of the women, as against 32 per cent. of the men, died.

Murchison has suggested that, as *alcoholism* is much more common in men, the difference in the sex death-rates is not unnatural, for there is no doubt that alcoholics have an extremely poor chance of recovery. In them the ataxic symptoms of the fever are liable to be much exaggerated, and their resistance to the poison is altogether much weakened. It is also a fact that the greater muscular development of men is very much to their disadvantage in this fever. I have always noticed that it is the large, heavy,

and muscular men who die, the fever being usually much less fatal to those of a slighter physique, a fact also remarked upon in Serbia by Chesney. Fat persons also, whether male or female, very frequently succumb, and one cannot resist the conclusion that *heavy weight*, whether from muscle or fat, is against the chances of a patient's recovery.

The condition of the *nervous system* is also of much importance. A patient who sleeps well, who has no subsultus tendinum, and who is able to be roused sufficiently from his lethargic condition to put out his tongue when asked, will be likely to recover. On the other hand, severe nervous symptoms, especially either wild delirium or coma, are of evil omen. None of my patients who suffered from delirium ferox recovered. Again, such symptoms as picking at the bedclothes, twitching of the facial muscles, or choreic movements of an almost convulsive character, point to a very bad case. As regards the *pulse*, so long as it remains below 120 there is always a good hope of recovery; if it exceeds 130 the outlook is extremely serious. Respirations exceeding forty per minute, especially if accompanied by marked cyanosis, are of grave import. Flapping of the alæ nasi on inspiration is a very bad sign.

The *rash* also gives a direct indication as to the severity of the case, profuse eruptions, with many petechiæ, showing that it is likely to be a serious one. On the other hand, a scanty rash, not much stained into the skin, and disappearing after a few days, suggests a mild attack. Without being a very ardent believer in the old views about critical days, I am inclined to think that there is something to be gained in the way of prognosis by a careful study of the *temperature* chart about the seventh day. A very large number of my charts show a slight fall of temperature at that period, and some cases seem to commence, as it were, a slow lysis from that time to the thirteenth day, when the drop in the temperature becomes more abrupt. Such a gentle decline of the pyrexia is always a good sign, though occasionally it may lead to false hopes, if depended upon too absolutely. During the fever a chart which shows a fair morning remission, even of one degree, must be regarded as satisfactory. Should the temperature show signs of rising, rather than falling, at the time when the crisis is naturally to be expected, there is great cause for anxiety, especially if the rise reaches the level of 106° F. Such an elevation is too often the immediate precursor of death. Much *sweating* at the time of the crisis is, in my experience, one of the worst of prognostic signs.

TREATMENT. The first precaution to be taken is to free the patient from all vermin. Considering the overcrowded home conditions from which typhus patients usually come, nothing is more likely to do them good than the

supply of an abundance of *fresh air*. Large and airy wards, then, are requisite, and it is advisable to allow more cubic space per bed than is considered necessary for the other infectious fevers. It is as well to keep all available windows widely opened, and there need be no fear at all of the patients catching cold. Fever patients never catch cold, and those suffering from typhus seem to make excellent progress even if nursed in what might be fairly described as a gale of wind.

While the temperature remains high the bedclothes should be very light, a single sheet and blanket being a quite sufficient covering. The wards should be kept so far as is possible at a low temperature. Patients treated in this way probably obtain all the advantages and have none of the risks of a cold bath treatment, and I am convinced that this slight surface cooling is for their benefit. Even when in winter the temperature of our wards has been as low as 45° F. I have never had a complaint of cold from a typhus patient. How far such a method of treatment checks any tendency to hyperpyrexia I am unable to say, but it should, theoretically, exercise some control on the temperature. Hyperpyrexia is in my experience not very common in typhus, and I have never seen it occur in cases so treated except as a part of the death process. In addition to the effects of cold air, tepid spongings may be used frequently in cases whose temperatures run over 105° F., and indeed are comforting to the patient throughout the course of his pyrexia, whether it is severe or not. Antipyretic drugs are useless and dangerous. When the crisis commences the temperature must be carefully watched and extra bedclothes added, if necessary, to the bed. As soon as it is complete it is advisable to remove the patient to a convalescent ward, kept at a more genial temperature, and to allow him more liberal coverings.

To save exhaustion in patients who are constantly passing their evacuations under them, it is well to use night-shirts which open at the back instead of in front, and to leave the patient lying with the bare back next to the sheet. In this way the fatigue entailed by changing the shirt each time the sheets have to be changed is avoided, as the shirt, covering as it does only the front of the body, remains quite dry.

Typhus requires skilled *nursing*, and, if a nurse who has had experience of it cannot be procured, it is well to get one who has at least had training in nursing cases of typhoid fever. The mouth should be most carefully attended to and cleansed several times daily, the sordes being removed from the lips and teeth, and the tongue scrubbed and anointed with some antiseptic ointment, boracic acid and vaseline being a good preparation. The patient himself should be sponged with some dilute antiseptic at least twice a day, or more often if the case is severe and the odour well marked. In the

Edinburgh City Hospital Jeyes' fluid is used for this purpose, freely diluted in tepid water. Great care should be taken to see that frequent opportunities are given for micturition. Delirious patients do not ask for attention, and, as a result, are apt to suffer from retention. Cold water should be liberally supplied.

The forcing of large quantities of *water* upon the patient, indeed, is probably as satisfactory a method of systematic treatment as can be recommended. I have obtained admirable results by securing the ingestion of from 6 to 10 pints daily. To reach the higher figure requires an exceedingly conscientious and energetic nurse, as much tact and patience are necessary to persuade delirious patients to drink so copiously. The amounts of water mentioned are to be understood as extra to the ordinary fluid nourishment given, which under ordinary circumstances would never be less than 3 pints. The effects of this treatment are the marked diminution of toxic symptoms, such as delirium, insomnia, and subsultus, and the improvement of the condition of the mouth and tongue. I believe also that the temperature is to some extent favourably affected. It may be assumed that the toxæmia from which the patient suffers is diminished by the free excretion of toxins, made possible by the increased diuresis.

As regards *diet* it must be remembered that the digestion is usually very weak owing to the continued high fever. A fluid régime is, therefore, a necessity, and it is well to feed very much on the lines recommended for severe cases of typhoid fever in the acute stage. Milk, then, forms the best staple food, and should be given in measured quantities at measured intervals. Beef-tea, made somewhat strong to secure a stimulating effect, may also be given freely, provided there is no tendency to diarrhoea. Fluid extracts of meat, chicken jelly, plasmon, or other similar preparations can also be administered in moderate quantities. Egg-flip with a dash of brandy is also useful. After the crisis the appetite rapidly returns and solid food may be allowed as soon as it is desired, a light meal of white fish or a lightly poached egg with dry toast being suitable articles of diet to commence with. Butcher's meat may be given early in convalescence.

The question of stimulation is always important. It is not by any means always necessary to give alcohol as a routine. If, however, the medical attendant is in doubt, it is safer to allow it. Hot beef-tea will, in many cases, be quite sufficient to stimulate the patient, and should in every case be tried first. But it must be admitted that the majority of adult patients require alcohol at the time of their crisis, even if they have not done so earlier. Three-quarters of my own adult cases certainly needed it. On the other hand, I have not found it necessary in more than one-third of the

children whom I have treated. Whisky is probably the most reliable form of stimulant, but in cases where there is sickness or diarrhœa brandy is to be preferred. If, as happens particularly in alcoholic cases, the alcohol fails to improve the pulse sufficiently, cardiac tonics, such as digitalis and strophanthus, may occasionally be of service, though too often they will be found disappointing. Strychnine is often useful, but, if there is much insomnia or marked ataxic symptoms are present, it increases the restlessness and jerkiness of the patient too much to be a desirable drug to employ, and if there is diarrhœa its use also is contra-indicated. Camphor in oil may be found more satisfactory.

Suitable hypnotics must be used to combat excitement and *sleeplessness*. It is often difficult to decide what is the best drug to use. For my own part I have had better results with sulphonal, in doses of 25 to 30 grains, than with any other hypnotic. If the pulse is very poor, paraldehyde is probably safer, and, if given with sufficient freedom, up to 5 or 6 drachms, is quite frequently successful. It is highly important to give these drugs early and freely. If the patient is allowed to have more than one sleepless night it is sometimes quite impossible to secure him a night's rest, and it is just these sleepless cases which are apt ultimately to present the symptoms of delirium ferox. It is better, therefore, if the patient appears at all excited when he first comes under observation, not to wait to see if sleep comes, but to secure it with certainty by an adequate dose. Once a drug has been given it must be repeated, or supplemented by another, after a reasonable interval. Otherwise, if it has not acted, the excitement or sleeplessness will be aggravated by it. If sulphonal after four hours has failed to act, I give 2 drachms of paraldehyde, and this combination is often effective. If paraldehyde does not produce sleep it should be repeated in drachm doses every half-hour till the desired result is attained.

In the wild excitement of delirium ferox restraint of the patient is often necessary. Nurses are otherwise quite helpless, and the omission of due precautions may mean danger to them and perhaps death by suicide to the patient. Some cases may be effectively controlled by a sheet across the chest with the ends tied under the bed. As a rule, however, it is safer to use straps with wristlets and to secure the patient to the bed. Drugs are seldom of any use in these cases, but of course must be tried, sulphonal being used for choice, and, if it fails, hyoscin hypodermically. Murchison speaks on the whole favourably of the use of opium, but, as he admits that it is contra-indicated when the pupils are persistently contracted or the lungs engorged, there are really very few opportunities for its employment except in the young, to whom it is probably not very safe to give it. Chloral, which he

also recommends, does not seem to me a particularly safe drug in a disease in which there is marked degeneration of the myocardium and frequently much cyanosis. It is, however, useful, when used with caution, for those patients who present much muscular tremor or convulsive twitching.

Constipation nearly always requires treatment during the first eight or ten days of the fever. It is safest to use enemata or very moderate, say one and a half drachm, doses of castor oil. I have seen intractable diarrhoea follow too large doses of aperients, particularly if given late in the disease. For *diarrhoea* it is best to first stop any beef-tea or similar preparation which the patient may be having, and to restrict the diet to boiled milk diluted with limewater. Occasionally chalk mixture or an astringent may be required.

Another distressing symptom is *headache*. This is sometimes much relieved by a five-grain powder of citrate of caffeine, which I prefer to phenacetin or antipyrin, as it has not the same depressing effect upon the temperature. Evaporating lotions, or an ice cap to the head may also be of service, and there is no doubt that the latter is also useful in conditions of excitement and delirium.

Should *coma* supervene, strong coffee is of some value. Blisters to the nape of the neck have also been advised, but are not without disadvantages. Still in such a desperate condition their use is quite justifiable.

Keeping in mind the frequency with which *retention of urine* is met with in this fever, great attention must always be paid to the condition of the bladder, especially in the case of delirious patients. A routine percussion of the organ twice daily, and the frequent encouragement of the patient to pass water, will save a great deal of subsequent trouble with the catheter. When the use of an instrument becomes imperative, it is advisable to draw off the urine at least every twelve, and preferably every eight, hours. It must be remembered that nurses may report that a patient is passing large quantities of urine into the bed, and yet the bladder may be much distended, the soaking of the sheets being merely the result of an occasional overflow. The discomfort and restlessness caused by such a state of affairs are highly prejudicial to the patient, quite apart from the risk of the occurrence of cystitis.

It may be well to mention certain *systematic treatments* which I have had no opportunity of testing. Oufugeaninoff recommends the internal administration of iodine, of which he speaks very highly. Danielopolu uses intravenous injections of chlorine water for severe cases, and therefore it might be reasonable to try eusol, although my experience of that preparation in other acute conditions has not been very favourable. Intravenous injections of electrargol and of colloidal gold have also been employed, a method too

hazardous if myocarditis is suspected, as its benefits depend largely on shock and subsequent leucocytosis.

Specific Treatment. Legrain and Treille report good results from the injection of *convalescent serum*, taken from thirty-six to forty-eight hours after the crisis and administered in doses of 30 grammes. Nicolle and Blaizot have been successful in immunizing the horse and the ass, and have used a *serum* from this source for hypodermic injection in doses of from 10 to 20 c.c., given daily until defervescence. It is improbable that this serum is procurable, but it appears to have given encouraging results.

PROPHYLAXIS. The opening up of air spaces in the crowded slums of our great cities, the regulation of common lodging-houses, the pulling down of old tenements, and sanitary supervision generally, have already made large epidemics of typhus practically impossible in civilized communities. Further steps in the same direction, such as the prohibition of one-roomed dwellings, the compulsory cleansing of common stairs and landings, and the prevention of overcrowding, will do much to prevent the possibility of the occurrence of even small outbreaks. Should, however, such outbreaks occur, the best method of dealing with them is, firstly, the compulsory *isolation* in hospital of all who suffer from the disease, a precaution which is essential under all circumstances. Secondly, all persons living in the same house, and all friends or neighbours who have been in close communication with the patient, should be kept in *quarantine* for at least fifteen days. On admission a very careful 'de-lousing' process must be carried out, and it will be well to assume that all lice, of whatever variety, are dangerous. The contacts must be bathed and their clothes, if not destroyed, disinfected by steam. Attention should be paid to nits and, if possible, very verminous persons should be shaved. Until thorough cleanliness is secured, attendants and nurses who have to deal with the sick or their contacts should perform their duties with rubber gloves drawn over the wrists of a 'combination' overall garment, which can also be tucked into the boots. As an additional precaution a little petrol or kerosene can be rubbed over the body. Once the patients are 'de-loused' such means of protection should be unnecessary in a clean and modern hospital. In Edinburgh in old days, when the significance of vermin was not appreciated, it was always the nurses who received and bathed the patients who took the fever. Infection subsequently appeared to be rare. I prefer to keep quarantined contacts in bed, so as to avoid infection in the reception house, and any one with a rise of temperature should be at once placed under observation.

The *disinfection* of the houses and personal effects of patients and contacts is very necessary. This is not difficult in civil life. Under war conditions

disinfection may be almost impossible to carry out thoroughly, but great success seems to have been attained by the use of current steam from a railway engine, the clothes of a unit being disinfected in railway vans while the men are being bathed.

As regards specific prophylaxis attempts have been made to secure immunization by the injection of serum from infected guinea-pigs. Plotz has prepared a vaccine of his bacillus, but, until the latter is recognized as the cause of typhus, this can hardly be recommended. Otto and Rothacker have used the blood of typhus patients, taken either at the height of the fever or shortly after the crisis, for prophylactic injections, three doses of from 2 to 4 c.c. being given. They found that while this method had no effect in preventing infection, the mortality of the men thus inoculated was very much less than that of the unprotected. Külz seems to have had similar results. Pecirka and others have recommended quinine as a prophylactic.

CHAPTER IX

ENTERIC FEVER

Nomenclature.

Etiology : bacteriology, the bacillus typhosus, predisposing conditions.

Dissemination and Infection : water, milk, food substances, air, dust, flies, fomites, direct infection, 'carriers'.

Pathology and Morbid Anatomy.

Period of Incubation.

Period of Invasion : symptoms of the first week.

Course of the Temperature : the onset, the continued stage, the lysis.

Period of Advance : symptoms of second and third weeks.

Analysis of the Principal Features of the Period of Advance : appearance, tongue, abdomen, eruption, stools, pulse, respirations, nervous symptoms, urine, blood, skin.

Period of Defervescence.

Period of Convalescence.

Results of Typhoid Ulceration : hæmorrhage, perforation, diarrhœa, meteorism.

Relapse.

Post-typhoid Pyrexia.

Varieties of Enteric Fever : mild and severe types, apyrexial typhoid.

The Paratyphoid Fevers.

Complications and Sequelæ : thrombosis, pneumonia, laryngitis, parotitis, peritonitis, typhoid spine, &c., &c.

Enteric Fever and Pregnancy.

Diagnosis : differential diagnosis from pulmonary, tubercular, abdominal, and other conditions.

Subsidiary Methods of Diagnosis : the diazo reaction, blood counts, bacteriological diagnosis, the serum-reaction test.

Prognosis and Mortality : age, sex, appearance, pulse, temperature, ulcerative complications, relapse, &c.

Treatment : Management : Diet : liberal feeding, scientific feeding, low feeding : expectant treatment, treatment of individual symptoms, stimulation.

Systems of Treatment : antiseptics, antisepsis by elimination, water drinking, the cold-bath treatment, serum and vaccine treatment.

Prophylaxis.

Subvarieties—Typhoid Fever, Paratyphoid Fevers A and B.

Synonyms—Typhoid Fever, Gastric Fever, Infantile Remittent Fever, Pythogenic Fever. *French*, Fièvre typhoïde, Dothiémentérie. *German*, Abdominaltyphus.

NOMENCLATURE. The name officially given to this fever, *enteric*, is, no doubt, not entirely satisfactory. It gives a somewhat undue importance to the intestinal inflammation, which, though usually present in a greater or less degree, is in no way responsible for many of the most serious symptoms of what is, after all, a general infection. The more popular term, *typhoid*, has perhaps even greater disadvantages. All it implies is that the fever bears in its symptomatology a considerable resemblance to typhus, and

that many patients suffering from it pass into the 'typhoid state', a condition liable to be met with in most of the acute infections. Murchison, believing that the disease could originate *de novo*, from the mere putrefaction of sewage, suggested the name 'pythogenic fever', a term which has met with no support. It is probable that the name 'typhoid fever' will be always that most frequently used, but it is none the less very desirable that this title should be reserved for cases due to infection by the bacillus typhosus, while the name 'enteric' is kept as a generic term to include also infections by the two paratyphoid organisms. From a public health point of view there is no particular advantage in emphasizing the bacteriological distinctions, and clinical differentiation must be usually impossible. It is only in treatment and prophylaxis by specific means that the exact variety of the causative micro-organism becomes of importance.

The distinction between typhus and enteric was not finally made till the middle of the nineteenth century. On the other hand, Louis, in his classical work published in 1829, had given an admirable description of enteric under the name of 'fièvre typhoïde'. To Gerhard of Philadelphia, Stewart of Glasgow, and lastly to Jenner, the credit of the final differentiation of the two fevers is due.

ETIOLOGY. Bacteriology. Eberth, in 1880, succeeded in finding small masses of bacilli in the Peyer's patches, mesenteric glands, spleen, and other organs of a series of fatal cases of enteric fever. His claim that these bacilli were the cause of the disease was supported by the experiments of Gaffky, who investigated their life history, and succeeded in cultivating them upon various media. Other observers have caused death in small animals by the injection of pure cultures of this bacillus, and Remlinger succeeded in producing a disease, closely resembling the fever as it occurs in man, by feeding rabbits on lettuces sprinkled with water containing the bacillus. Similar results have been obtained by Grünbaum, and more convincingly by Metchnikoff and Besredka, working with chimpanzees. It is, perhaps, not possible to assert with any certainty that the condition so produced is identical with enteric fever, but it must be remembered that animals do not in nature suffer from the disease, and that, therefore, the symptoms of infection may present some differences from those observed in man. As apart from this point, however, the evidence in favour of the bacillus typhosus being, in reality, the cause of the fever is extremely strong. The micro-organisms are found in the organs of those who have died of the disease; they have not been isolated except from such cases. Further, they have been detected in water which has been apparently responsible for outbreaks of enteric, and again, instances of bacteriologists developing the fever, after

having accidentally infected the mouth with pure cultures, are not uncommon. Lastly, the protective qualities of the serum of enteric patients against typhoid bacilli inoculated into animals, the agglutination of the bacilli *in vitro* by the blood of such patients, and the protection afforded against the disease by the injection of dead cultures into the human subject, all point strongly to the bacillus of Eberth being the causative micro-organism.

The *bacillus typhosus* is a somewhat short thick rod with rounded extremities. In young cultures, however, elongated filamentous forms, as shown in the illustration, are frequently seen. It is actively motile, as may be readily demonstrated by the examination of 'hanging drop' preparations. The motility is due to the large number of long flagella with which it is provided. The detection of these requires special methods of staining. The bacillus itself stains well with carbol-fuchsin or carbolic methylene blue. It is decolorized by Gram's method. Cultures may be made on agar, gelatine, or bouillon. They should be incubated at 37° C., but grow slowly at ordinary room temperatures. A streak culture on agar shows a bluish grey film of growth with no special characteristics. A bouillon culture presents a uniform turbidity.

The chief difficulty with which we have to contend, when endeavouring to isolate the bacillus, either from suspected water or from the organs of an enteric patient, is the great resemblance which it bears to the bacillus coli communis. The fact that this latter micro-organism is normally present in the intestine, and multiplies rapidly when any intestinal disease exists, makes it impossible to differentiate the two germs in the stools or tissues by direct examination, and it is necessary to make cultures on various media in order to arrive at any definite conclusion. The difficulty is increased by the fact that many different bacilli, similar morphologically, and only to be recognized by the most delicate culture tests, may occasionally infect the human subject. In their characteristics these micro-organisms may resemble closely the typhoid bacillus, the colon bacillus, or both. The most important varieties in this intermediate group are the bacillus enteritidis of Gaertner and the paratyphoid bacilli, of which the two forms classed as A and B are well known, while a third, tentatively called C, has been recently described. The services of a skilled bacteriologist will in all cases be required to accurately differentiate the various micro-organisms, and a discussion of the methods employed may well be omitted from these pages. Agglutination reactions, carried out with standard serums, are usually required for the final differentiation of the paratyphoid organisms.

It is, however, important to note that the typhoid bacillus is killed by exposure to a heat of 60° C. for half an hour and of 100° C. for three minutes.

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PLATE XVIII.



BACILLUS TYPHOSUS. A twelve-hour culture on agar showing long forms.
×—1000. Fuchsin.

It dies out fairly rapidly in drinking water, probably within three weeks, and does not survive long in ice. It resists drying fairly well and, though it does not multiply in the soil, has been found alive after 74 days.

The bacillus is to be found in many of the internal organs. It probably occurs in greater numbers in the spleen and gall-bladder, but it is also often detected in the mesenteric glands and liver. In the early stages of the disease, before necrosis of the affected lymphoid tissue has commenced, it is present in the enlarged Peyer's patches of the small intestine. More rarely it has been cultivated from the lungs and the kidneys. During life it may be obtained from the stools, urine, and blood, and less commonly from the sputum and bilious vomit, of persons suffering from the fever. Advantage may be taken of this, as will be seen, as a means of diagnosis.

Very little appears to be known about the *toxins* produced by the bacillus typhosus. It was usual to assume that it only possessed an endotoxin, but it has been more recently stated that it can under favourable conditions set free also an exotoxin which, if not comparable to that of diphtheria, only differs from it in degree. It has been suggested that the two toxins have different actions and that the endotoxin is responsible for the changes in the Peyer's patches, but this view is not generally accepted. In any case the toxins may be regarded as the cause of the toxic symptoms presented by patients.

Predisposing conditions. Enteric fever has an extensive *geographical range*. It occurs in all parts of the world. Extremely common in temperate climates, it is frequently met with in the tropics. In most countries it is endemic, with occasional outbreaks of epidemic prevalence.

While the disease occurs at all times of the year in Great Britain, the most usual *season* for its endemic prevalence is autumn. It has been referred to, indeed, as 'autumnal' fever. In Edinburgh a rise in the number of cases is usually noted in the month of May, and a more marked increase occurs in September and October. An epidemic, however, may appear at any season.

Age. Enteric fever is a disease of early life. It occasionally, though rarely, occurs in infants, and is fairly common in the first five years of life. Between the ages of five and ten years there is a very marked increase in the number of cases. The great majority of patients, however, are from ten to twenty-five years of age. After twenty-five, the number of cases gradually diminishes to the age of forty. From that age the fall in the number of persons attacked in each five years of life is more rapid, and enteric fever is rarely met with after the age of sixty. In a table given by Goodall, only thirty-nine patients out of 21,371 were above that age.

Sex. Males are more frequently attacked than females. In Goodall's table they are considerably more numerous in every quinquennial period up to the age of forty-five. Thereafter, there is a slightly larger number of females than males in each succeeding period of five years. These differences cannot be entirely explained by the different occupations of the two sexes, for the predominance of males below the age of ten is sufficiently well marked.

Other predisposing causes. It is only natural to suppose that such conditions as fatigue, overwork, and life under abnormal conditions should predispose to the disease. The influence of these causes has been denied by no less an authority than Murchison, but my experience has taught me to remove from exposure nurses who appear to be overworked, or whose health is below par. Night duty, again, renders a nurse more liable to enteric fever, and this cannot be altogether explained by the conditions under which the food is taken. The frequency with which enteric relapses appear with the menstrual period suggests that resistance is low at that time, but I must confess that I have no data to prove that original infection is particularly probable during menstruation. Destitution and conditions of overcrowding certainly do not play the same part in the production of enteric outbreaks as they do for those of typhus, but recent observations go far to show that the crowding of soldiers in tents must do much to favour that personal infection which, it is now admitted, has to be seriously considered when epidemics are investigated. It has long been held that persons are most likely to contract enteric fever when they are brought into contact with it before they have become acclimatized. A change to new conditions of life and climate would certainly appear to predispose to the disease if the possibilities of infection are present. This particularly applies to troops in the tropics and on foreign service. Active military service, whether in standing camps or on the march, affords most favourable opportunities for the development of typhoid epidemics.

DISSEMINATION AND INFECTION. The bacillus typhosus is contained in the excretions of persons who are suffering, or have suffered, from enteric fever. Formerly the stools were alone considered dangerous. We now know that the urine also frequently contains the bacillus. Recently many instances have been reported of the bacillus having been isolated from the excretions of persons who were in perfect health at the time of examination, but who had, a varying number of years previously, suffered from an attack of the fever. This fact does much to explain the occurrence of sporadic cases of enteric, the cause of which may not be very obvious, and, as will be seen below, the so-called 'carrier' must rank with the actual patient as a possible source of infection. The bacillus, then, derived from

the excretions of a patient or carrier may be conveyed to the recipient by one of the following routes.

The fact that the bacillus is in many cases transmitted by **water** has long been recognized. The water may become contaminated directly by sewage, or defective drainage may allow leakage into a supply otherwise above suspicion. In the first case the population so supplied is likely to suffer continuously from a high typhoid incidence, as has been the case in many great cities in Europe and America. In the second an explosive epidemic may follow the accidental contamination as in the Maidstone outbreak. The presence of colon-like bacilli may be taken as presumptive evidence of the pollution of water by sewage. In many cases the actual proof of typhoid contamination may be wanting, but the part played by the water may be satisfactorily determined upon epidemiological grounds. The bacillus does not live long in running water, and rivers, therefore, tend to purify themselves. Outbreaks have been attributed to *bathing* in infected water, and the question of transmission by means of *ice* appears to have caused some anxiety in America. Chapin, however, concludes that there is very little epidemiological evidence that ice is the cause of sickness.

Many cases of **milk** contamination are, doubtless, due to the use of infected water for washing the cans, or even for the purpose of adulteration. Milk, as is well known, is very readily contaminated by germs, and several epidemics in this country have been traced to such a source. Often the contamination is due, not to infected water, but to the hands of some attendant who, either a carrier himself, or nursing an enteric patient at home, continues to milk the cows or to work in the dairy. The typhoid bacillus causes no visible change in the appearance of milk and, on the other hand, germs multiply rapidly in such a medium. As the milk from one farm is often distributed among a considerable number of milkshops in a large town, it can readily be seen how a widely spread outbreak may be caused by infected milk. Harvey Littlejohn has reported such an outbreak, which occurred in Edinburgh in 1890, sixty-three persons, residing in different parts of the city and supplied by seven milkshops, being attacked by the fever. Part of the supply of all these shops came from one farm, and one of the children of the farmer was found to be suffering from typhoid. In France and Prussia *beer* and *cider* have been found liable to contamination by carriers in a similar way.

Various articles of **food** are also liable to typhoid contamination, often, no doubt, from the water, milk, or soil with which they have been in contact, or which have been used in their preparation. Thus *celery* and *water-cress* have given rise to outbreaks, and *ice-cream* has also caused the disease.

The part played by *shell-fish* in the causation of typhoid epidemics has attracted much attention in recent years. Oyster-beds are often placed at the mouths of rivers and near sewage effluents, and thus readily become contaminated. The same applies to mussels and the smaller shellfish. Some years ago many of the cases admitted to the Edinburgh Fever Hospital were apparently due to the eating of raw mussels. A report by Buchan to the Medical Officer of Health of Birmingham showed that various micro-organisms, the presence of which might fairly be regarded as a proof of pollution, such as the bacillus coli and the bacillus enteritidis, were present in a very large percentage of shellfish offered for sale in that city. Chapin mentions some interesting cases presumably due to the eating of crawfish from polluted water. Outbreaks in London were traced by Hamer to particular *fried-fish* shops. It would at first sight appear impossible for germs to survive the process of frying, but it is conceivable that the heat did not penetrate sufficiently to sterilize any bacilli in the entrails.

At one time foul **air** was supposed to play a prominent part in the production of typhoid outbreaks. Our views on the epidemiology of the disease to-day do not permit us to favour such a supposition. It is not easy to see how the bacillus can get into sewer gas unless, indeed, the sewage dried in the pipes, but the bursting of small bubbles on the surface of liquid sewage is said to be capable of setting free the germs, and the carriage of bacilli in the air of the pipes has been demonstrated experimentally. On the other hand, Winslow has proved that sewage bacteria are but seldom found in sewer air, and then only in very small numbers and after mechanical splashing. The risk of infection by this means, then, would appear to be negligible. That the bacillus can be carried by **dust** must, I think, be admitted. Chour discovered it in the dust of a barrack-room in which the disease was endemic, and it can scarcely be doubted that the dust, so much complained of during the Boer war, was partly instrumental in disseminating the fever. The bacillus resists drying to a certain extent and has been proved to live in sand, for instance, for as long as twenty-seven days. Contamination of soil, then, dry weather, and an occasional dust storm would be sufficient to spread infection. Moreover, the dust of dried stools on a sheet, subsequently inhaled as the nurse disturbs the bedclothes, would in my opinion account for some instances of hospital contagion. In the case of patients with frequent small evacuations, passed involuntarily, the occasional rapid drying of one or more very small faecal stains can hardly be avoided.

The bacillus can also be carried by **flies** and perhaps also other insects. It is probable that many of the cases in the Boer war were infected in this manner. It is easy to see how a fly may first visit the latrines and then

crawl over the food of the troops. The insect not only carries the micro-organisms on its legs but also within its alimentary canal, and with its habits of regurgitation and frequent defæcation is particularly likely to infect food. But although attempts have been made to prove that an increase in typhoid incidence coincides with the prevalence of the common fly in this country, it is doubtful whether the fever is disseminated much by this method except perhaps in those towns in which privies, and not water-closets, form the sanitary arrangements. An interesting report of Dittmar's indicates that the comparatively excessive prevalence of enteric fever in the west of Scotland may be explained by the fact that, whereas the eastern towns have for long had a water-closet system, those in the west have depended largely on privies. He concludes that conservancy methods of dealing with human excreta favour the spread of enteric fever, and that this is due to the opportunities provided by these methods for repeated re-infection of the soil in the neighbourhood of dwellings and for the contamination of food by flies.

Such **fomites** as bed linen, blankets, and clothes soiled by enteric patients can also convey infection. Thus the fever has been given to laundresses and nurses. A supply of old army blankets, which had been in use in South Africa and which still showed fæcal staining, was responsible for an outbreak among the boys of an industrial school.

Contact Infection. Enteric fever is not, strictly speaking, directly contagious. That is to say, it is not contact with the patient himself, but rather with his excreta, which causes infection. But it is now recognized that the disease is certainly spread from person to person, a mode of transmission which for long was regarded as very improbable. The extreme rarity with which the fever infects patients suffering from other diseases in a hospital ward is no doubt due to the fact that, in well-regulated hospitals, there is little chance of typhoid excreta being carried, either on the hands of a nurse or otherwise, from the typhoid cases to the others. In twenty-three years, during which time hundreds of patients suffering from conditions other than enteric have been admitted to the typhoid wards of the Edinburgh City Hospital, I have only seen one instance of infection. Nurses, on the other hand, whose duties bring them in contact with the patient's evacuations not infrequently contract the disease, often no doubt from taking food with hands not surgically clean, sometimes, as has been suggested above, from inhaling the dust of fæcal spots on the sheets. In the volunteer standing camps in the United States at the time of the Spanish-American War the spread of enteric was shown to depend largely upon personal contact, the men who occupied the same tent contracting the disease from each other, or

at least from the dust of the tent floor and the clothes of those affected. In civil life, however, direct infection appears to be somewhat unusual, the number of houses supplying more than one case being relatively small, except when the cause of the outbreak is a defective water-supply, or when the conditions of living are exceptionally unfavourable. Among the poorest classes it is certainly not uncommon to see a whole family affected by the fever, the individual members being admitted at intervals to hospital.

An undoubted source of danger is the so-called **carrier**. A person who has had the disease may harbour the bacillus in his gall-bladder or elsewhere, and his stools and urine may be infectious for an indefinite period. Even persons who have not suffered from the fever appear capable of being carriers for a longer or shorter time. According to statistics given by Ledingham women furnish by far the larger number of chronic carriers, and the figures suggest that the condition is much less frequently met with in children than in older persons, the elderly, indeed, showing a comparatively large proportion. Although the expression 'intestinal carrier' is often made use of, there is reason to believe, says Cummins, 'that in the typhoid carrier, whether intestinal or urinary, the bacillus typhosus leads a parasitic existence in infective foci in the tissues, and that the fæces and urine are merely vehicles for its transmission to the outer world.' The bacilli are harboured in the bile, the liver, and the wall of the gall-bladder, and they are not infrequently associated with cholecystitis and the presence of gall-stones. Cummins states that, in the case of operation on urinary carriers, tissue lesions have always been found either in the shape of small abscesses in the kidney or of ulcers in the urinary bladder. In some carriers the lesions are periosteal deposits which may remain harmless for many years only to become active with the formation of an abscess, and infection from such a source has been reported. Carriers may be only intermittently infectious, that is to say in the case of the so-called intestinal carrier bacilli cannot always be recovered from the stools. Urinary carriers, on the other hand, appear to 'intermit' much less frequently.

The carrier may be dangerous both to those who in any subsequent illness have to do with the disposal of his excreta, and to the public generally by fouling the ground with urine containing bacilli. Most of the reported cases have been persons whose duties connected them with the preparation of the food of other people: cooks, dairy workers, mothers of families, and the like. Their power for mischief depends to a great extent upon their habits, cleanliness, and surroundings. Want of cleanliness after micturition or defæcation is apt to leave germs on the fingers, and Cummins had little

difficulty in recovering the bacillus from the fingers of known carriers. His experiments, moreover, showed the extreme difficulty of disinfecting by repeated washings a finger dipped in the urine of a carrier. Conditions of life on active military service are particularly favourable to the dissemination of the fever by means of carriers. It may be added that the agglutination reaction has been found to be most marked in these persons when they are most dangerous, i.e. when they are excreting most bacilli. Persons have been found to be carriers more than thirty years after an attack of the fever. It may be well to note that the paratyphoid bacillus can be 'carried' in the same way.

PATHOLOGY AND MORBID ANATOMY. Whether the bacillus finds its way into the human subject in water and food substances, or whether it is inhaled through the nose in the form of dust, it probably in the vast majority of instances obtains its first nidus in the alimentary canal. The view most generally accepted has been that the germs multiply in the intestine, cause inflammation of the lymphoid tissue, and, ultimately entering the circulation, produce the general septicæmia which must be admitted to be the outstanding feature of the disease. Sanarelli has suggested that the disease is primarily general, and that the intestinal lesions are due to the excretion of toxic substances produced elsewhere. Others again, disbelieving the multiplication in the intestine, hold that the bacilli gain entrance to the general circulation through the tonsils, multiplying in the blood, and also in the gall-bladder to which they obtain access. From that situation they are alleged to pass to the intestine. Another theory suggests that reaching the intestine first they are carried to the gall-bladder by the portal circulation and in the favourable medium of the bile multiply sufficiently to reinfect the intestine more seriously. The necrosis of the lymphoid tissue may well be due to a mixed infection. It is not impossible the bacillus coli may play some part in this, and recently Molikoff has suggested that an anaerobic micro-organism, which he has termed the bacillus satellitis, is responsible for the necrotic changes, while the bacillus typhosus causes the septicæmia. It is well in any case to remember that cases presenting during life the classical symptoms of the fever have been found after death to show a perfectly normal intestine, even although pure cultures of the bacillus have been obtained from the blood, spleen, gall-bladder, lungs, or elsewhere. The cases, to be described afterwards as pneumo-typhoid, meningo-typhoid, and so on, may be instances of the primary focus of infection occurring in the organ concerned, and occasionally the bacillus seems capable of restricting its action to one particular organ. Thus, in a patient under my own observation, the lesions were limited entirely to the meninges, and there were no symptoms

of 'typhoid fever' during life, but the only germ present was the bacillus typhosus.

The most **characteristic lesions** are those of the *Peyer's patches* and solitary glands in the ileum, the last few feet of the gut above the cæcum being affected most. The first change in the lymphoid tissue is apparently due to *infiltration* with leucocytes. The patch becomes somewhat pink in colour, and is gradually raised above the level of the surrounding mucous membrane. The lesions show a varying degree of hardness, some being very soft and of a dark red colour when they are fully developed, while others are paler, firmer, and more raised above the surface. French authors have distinguished these by the names of 'plaques molles' and 'plaques dures' respectively, but the distinction is of little importance as the process is apparently the same in both cases.

After this process of infiltration has continued for a period which varies in duration in different cases, the second stage, that of *necrosis*, commences. The enlarged mass gradually sloughs away, either as a whole, or more frequently in detached fragments. It is probable that this change begins about the tenth or twelfth day of the fever, and that in abortive and mild cases it is dispensed with altogether, the gland resuming the normal by a process of absorption. If necrosis does occur, the sloughing mass becomes greyish in colour, and is frequently stained a bright yellow on the surface.

The separation of the slough is usually complete by the end of the third week, by which time the typical *typhoid ulcer* is formed. The ulcer may show a varying degree of depth, the muscular coat being not infrequently involved, while occasionally the base is formed by the peritoneal coat completely denuded. In shape it usually corresponds to the outline of the Peyer's patch itself, but, if the gland sloughs only in part, it may assume very irregular forms. Its coalescence, moreover, with other ulcers or with diseased solitary glands may present an ulcerated surface of considerable extent and irregular outline. It may be distinguished from tubercular ulceration by its long axis being parallel to that of the bowel, and its primary situation being opposite the peritoneal attachment of the gut. Its edges, moreover, do not show that induration which is so characteristic of both base and edges in the tubercular ulcer.

The typhoid ulcer has three possibilities before it. It may, and usually does, undergo a process of repair, it may become chronic and exist several weeks before healing, or, lastly, it may perforate. If healing takes place, small granulations appear upon the surface and these are gradually covered by the mucous membrane growing in from the edges. Very little true cicatricial tissue is formed, and, as a result, there is no tendency to con-

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TYPHOID ULCERATION.



traction of the gut. A few weeks after the disease has terminated all that can be seen is the so-called 'shaven beard' appearance, minute black dots on a greyish surface. The glandular tissue, however, is not restored.

Perforation may occur in three ways. Firstly, and usually, there may be a gradual extension in depth of the necrotic process, which ultimately reaches the peritoneal coat and works through it. In such a case the perforation is small; hardly larger, indeed, than the head of an ordinary pin. Secondly, the whole Peyer's patch, including the whole thickness of the tissues beneath it, may slough completely away, and, as it were, drop out, leaving an opening corresponding to the size of the gland itself. Lastly, in certain cases, where the slough has separated and where the floor of the ulcer is formed merely by the peritoneal coat, the latter may give way and present the appearance of having been torn across.

In looking for a perforation post mortem, great care must be exercised in the handling of the bowel. In such cases there is always more or less peritonitis, and flakes of purulent lymph occasionally hide the lesion. Before removing the bowel it is advisable to examine the most acutely inflamed parts *in situ*, gently wiping off any adherent lymph with a sponge. Attention will first be paid to the last two feet of the ileum above the ileo-cæcal valve, the vast majority of perforations occurring in that locality. If, after removal, the bowel is flushed through under a tap, artificial perforation may readily occur. It is safer to open the gut without flushing it, allowing merely a gentle stream of water to trickle over it and wash away the fæcal matter.

As regards *other intestinal changes*, a similar process to that detailed above takes place in the solitary glands. Occasionally, indeed, these glands alone are affected, the Peyer's patches completely escaping, thus giving rise to what has been termed the pustular form of the inflammation. In many instances the glands of the large intestine also ulcerate, particularly those in the neighbourhood of the ileo-cæcal valve, but ulceration may occur at almost any point of the large intestine. The lesions, indeed, may be limited to the large intestine, and in one of my cases death was due to profuse hæmorrhage from the cæcum, the small intestine showing no ulceration at all. The appendix is sometimes ulcerated, and perforation may occur in this situation. The mucous membrane of the intestines is frequently brightly injected, and the position of the ulcers may be marked on the external surface by patches of deep congestion. Occasionally the inflammation is so intense that large pieces of the bowel become absolutely gangrenous. I have seen this occur both above and below the valve. In prolonged cases the bowel-wall shows very marked thinning and atrophy.

The *mesenteric glands* are always enlarged, often to a considerable extent. They are pinkish in section and are sometimes softened and diffuent in the centre. The *spleen* is dark in colour, and almost invariably is much enlarged, being often three or four times its natural size. Occasionally it is diffuent. The heart shows degeneration of the cardiac muscle, with occasionally marked thinning of the walls. It is usually pale and flabby. The other organs present no special changes, beyond what may be expected in cases of acute toxæmia, though ulcerations are sometimes found in the larynx and pharynx, and the lungs of severe cases may show more or less hypostatic congestion.

If cultures are desired, there is a fair chance of obtaining them pure from the gall-bladder; when taken from the spleen or mesenteric glands there is a greater probability that they will be contaminated with the *bacillus coli*.

COURSE OF THE FEVER. Incubation. This period is extremely variable and, so far as can be judged, depends to some extent on the amount of the virus taken. Perhaps about fourteen days is the most likely time, and from one to three weeks will cover the ordinary limits. Longer periods, however, have been reported, one by Vincent of a laboratory infection with a latent stage of forty days. With all deference to well-informed criticism, I think we must also admit that incubation periods of less than a week are quite possible, and intervals of two, three, four, and five days have been noted in recent literature.

It is asserted that enteric fever, unlike the other acute infections, presents certain symptoms of headache, loss of appetite, and lassitude in this period. If that is in reality the case, the term 'stage of incubation' is a misnomer. A few patients certainly appear to suffer from symptoms at the presumed moment of infection, but this might be readily accounted for by the food or liquid ingested being contaminated with other micro-organisms, as, indeed, must often be the case. The extremely insidious character of the commencement of the actual fever has, no doubt, caused certain symptoms to be attributed to the incubation stage, which, in reality, formed part of the period of invasion.

Stage of invasion. The duration of this period may be said to be from the first complaint of the patient to the moment when the gradually rising temperature has reached its acme. The insidious nature of the onset often makes it very difficult to determine with any accuracy the exact day on which the febrile process starts, but in most cases it is probable that the invasion stage does not last less than a week. Sometimes the onset is sufficiently well indicated by an attack of shivering, which, however,

is seldom severe enough to merit the name of a rigor. But, as a rule, the first complaint of the sufferer is that he feels out of sorts. In addition to this sensation of *malaise* the most constant symptom is probably *headache*. This is usually frontal in character, and, in comparison with some of the other fevers, is not exceptionally severe. Occasionally it assumes a neuralgic type and may be limited to one side of the head. Pains in the back and limbs are often complained of. Feelings of chilliness are not uncommon in this early stage of the fever, and some patients suffer much from giddiness. *Insomnia* is a frequent symptom, and head symptoms and delirium at night are often seen, especially in young children. The tongue becomes furred, the mouth is dry and uncomfortable, and the appetite is often completely lost. The digestion is enfeebled, and there may be occasional attacks of vomiting. Many patients complain much of thirst. Sometimes perspiration is very profuse, and it may be followed by the appearance of a sudaminal rash. The urine is diminished in quantity, febrile in character, and, towards the end of this period, usually shows the diazo reaction of Ehrlich.

The symptoms detailed above are, it will be noticed, for the most part those which might be expected to be present in any acute febrile condition. In addition to them, however, there are usually some signs which point more directly to the nature of the infection. Of these, perhaps, *abdominal pain* or *discomfort* is the most constant. Few patients fail to present this symptom, and, if the abdomen is examined, tumidity and tenderness on pressure will be often found present. The bowels are almost always deranged. *Constipation* is probably more common than *diarrhœa*, but one or the other is usually present. A symptom which occurs with comparative frequency is *epistaxis*, and this may be noted as early as the second or third day of illness. Some patients suffer much from cough, often of a hard and dry character, but sometimes accompanied by bronchitic-looking expectoration. Any of these symptoms, taken in conjunction with the febrile manifestations noted above, should cause the idea of enteric to cross the mind of the attending physician.

During the stage of invasion the temperature, as a rule, rises in step-like gradations, with a well-marked morning remission (Fig. 32). But in some cases the onset of the fever is abrupt, and the acme may be reached in one or two days. Abnormal types of onset may also be observed in patients in whom important organs such as the lung or kidney are attacked from the first. The respirations are accelerated in proportion to the amount of pyrexia. The pulse, however, remains in most cases relatively slow.

COURSE OF THE TEMPERATURE IN ENTERIC FEVER. The fever, in the majority of patients, approximates to a very definite type.

For the first week of illness, the period of *invasion*, the temperature is *ingravescent*, slowly mounting to the *acme*. Each morning the level is higher than that of the morning before, though lower than on the preceding evening. This gradual rise doubtless accounts for the patient being able to keep his feet so long. He can, as it were, acclimatize himself to the change in the temperature level, whereas in most other fevers the rapid rise to the *acme* causes early prostration.

When the temperature has ceased to rise further, the patient enters the *fastigium*, or *period of advance*, during which the *pyrexia* is more or less

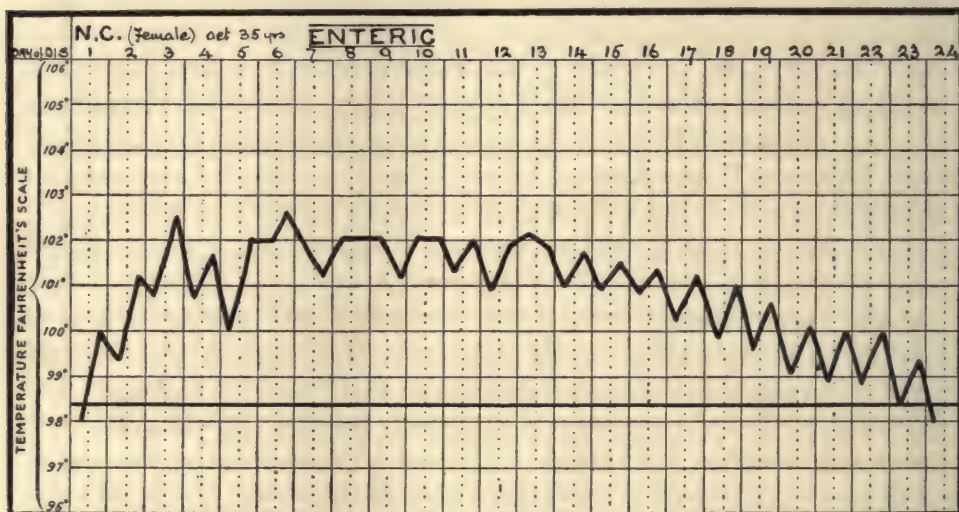


FIG. 33. A case of enteric fever from the first day, showing a somewhat short invasion period with step-like gradations. The stage of advance presents a temperature with but little tendency to morning remission, and is therefore of a relatively severe type. The pulse, however, never exceeded 104. Characteristic lysis.

of a continued type. An average level for this stage of enteric fever is from 101° to 103° F. Much higher readings, however, will be met with in certain cases. A morning remission usually takes place, the variation of temperature being from half a degree to two degrees. It is not unusual in severe examples of the fever to see but little morning remission (Fig. 33), and this is especially apt to be the case if the period of advance is continued into the third and fourth weeks of the illness, and if there is much and deep ulceration present. In favourable cases, however, the end of this period is often characterized by longer remissions. Marked variations between the morning and evening levels are most frequently seen in children, and this peculiarity is responsible for one of the synonyms of the fever, 'infantile remittent'. To obtain an

accurate knowledge of the extent of the remissions, it is necessary to take the temperature every four hours.

The third stage of the fever, *defervescence*, may commence at almost any time, though not usually before the beginning of the third week. The return to normal is as gradual as the rise, enteric fever furnishing the most perfect example of a lysis (see Fig. 34). It is seldom that this lysis is completed in less than a week, and not infrequently it lasts ten days or

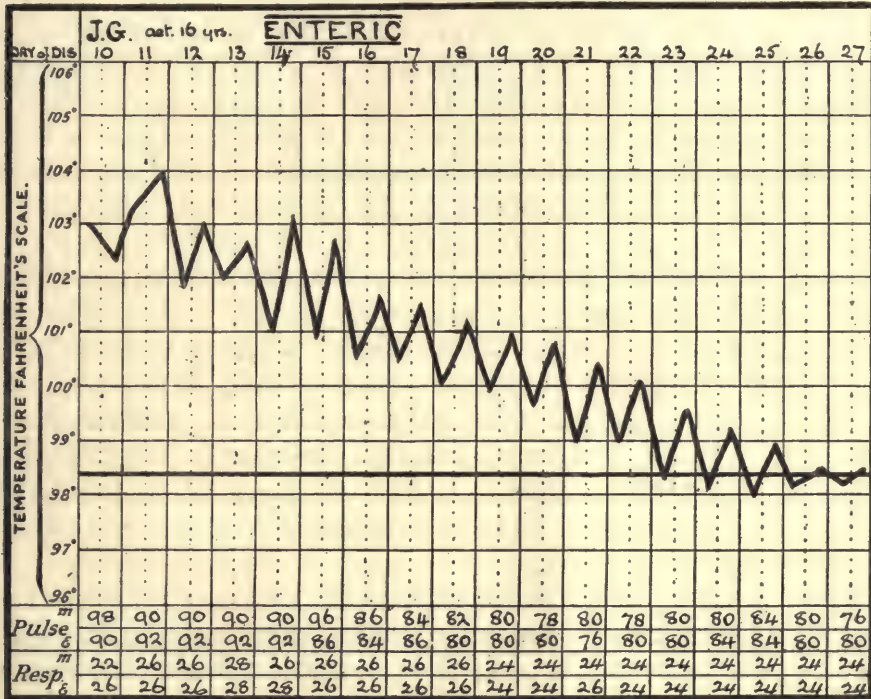


FIG. 34. Showing a very regular lysis. Note also the moderate pulse-rate in the earlier stage.

a fortnight. In some cases the fall each morning is very slight, and there may be but little difference in the level of the morning and evening readings, though the latter in the great bulk of patients is distinctly higher. Others, again, show a return to the normal by long morning remissions (see Fig. 43), the evening temperature at first maintaining the level of the fastigium, and only gradually declining after the morning temperature has been normal for some days. This type of defervescence is most commonly seen in young adolescents. In very rare instances an abrupt and almost critical fall may take place, the pyrexia completely subsiding within forty-eight hours.

I do not remember seeing this mode of termination on more than half a dozen occasions.

Even when the temperature has regained the normal it remains remarkably mobile for a week or ten days. A slight degree of constipation, or an apparently insignificant addition to the diet, will often cause a swing upwards of the evening temperature. This is less likely to occur, however, if the readings are once steadily subnormal.

While, in severe types of the fever, high levels of pyrexia, 104° to 105.5° , are sometimes maintained for several days together, true hyperpyrexia is an infrequent occurrence. I have seen it, however, in the fourth and fifth weeks of the fever in association with definite rigors. Sudden falls of temperature, occurring during the course of the fever, are often to be explained by the occurrence of hæmorrhage or perforation. A drop, occurring unexpectedly, and not accompanied by any improvement in the pulse or otherwise, is rarely to the patient's advantage.

As will be seen later, it is possible for enteric fever to run a subfebrile or completely afebrile course.

PERIOD OF ADVANCE. During the first week the typhoid patient seldom takes to his bed, but about the commencement of the second he is usually compelled to give in. Quite frequently, therefore, it is not till the period of advance commences that a medical attendant is called in, and in a long series of cases I found the mean day of admission to hospital was as late as the eleventh of the illness. The stage of advance may be said to start with the commencement of the second week, and is prolonged one, two, or more weeks according to the nature of the case. The actual duration of the acute stage, no doubt, partly depends upon whether ulceration of the Peyer's patches follows their infiltration or not. Should no ulceration occur, the period of advance may last only six or seven days and the fever subside in the third week of the disease. Should, on the other hand, necrosis occur, the fever may be continued indefinitely for two or more weeks, the longest period of advance which has come under my notice having lasted as long as seven. In the great majority of cases, however, the period lasts either one or two weeks, the complete illness being of either three or four weeks' duration. For convenience it will be well to first describe the conditions of the patient in the second week of illness, and then to give some account of the symptoms in those cases in which the fever is more prolonged. Thereafter the more important manifestations of the disease may be with advantage examined in detail.

In the *second week* of the fever, then, the patient has usually taken to his bed. He is listless and apathetic and may still suffer from headache.

Unless the attack is a severe one, he can still move in bed with comparative freedom. The tongue is furred, and usually dry, and there is absolutely no desire for food. Sleep is often broken and disturbed, and persistent insomnia is apt to be present at this stage. In such cases there is usually some delirium at night. Many patients suffer from deafness, and this, as well as their mental apathy and dullness, makes it impossible to obtain from them any satisfactory account of their early symptoms or of the dates on which they appeared. The abdomen is tumid, and not infrequently tender on pressure. The characteristic eruption of spots may or may not be present. The spleen is invariably enlarged. Diarrhœa is a frequent symptom of this stage, especially if the patient has not come early under treatment and thus enjoyed the advantages of careful dieting. The stools often assume the characteristic 'pea-soup' appearance. The pulse is of low tension and dicrotic, and is only moderately accelerated considering the height of the temperature. The morning remission of the latter is, except in extremely severe cases, well marked. The respirations are, as a rule, easy, and not particularly rapid. Occasionally a troublesome cough still persists.

It is with the beginning of the *third week*, always provided there are no signs of defervescence, that the dangerous stage of the fever sets in. A continued period of advance in most cases implies that the bowel lesions are entering on a stage of necrosis. The prolonged toxæmia, moreover, commences to affect both the nervous system and the heart. The patient becomes more stupid, and often suffers from a low muttering delirium. His tendons twitch, and he may lose control of his bladder and bowel reflexes. He has, in fact, entered the 'typhoid state', that condition, so much more common, no doubt, in the days before modern nursing, which used to cause enteric fever to be regarded as identical with typhus. The strength begins to fail, and, not infrequently, the patient lies constantly on the back, being unable to turn himself in bed. The pulse becomes rapid, and approximates more to the rate which the height of the temperature warrants. The tongue, if not attended to, is dry, glazed, and fissured, but the patient is too stupid to ask for the much-needed fluids, so stupid, indeed, that they sometimes must be forced upon him. The lungs are apt to become congested at the bases, and, as a result, the frequency of the respirations may be much increased. There is usually much loss of weight, the average patient being extremely wasted by the end of the third week.

During this acute stage fresh crops of spots may appear at intervals on the abdomen. Diarrhœa is occasionally severe, and towards the end of the third week shreds of sloughing material may be seen in the stools.

Meteorism is common, especially in cases which have come late under treatment. The ulcerative accidents of the disease may be looked for at any time after the middle of this week, and it is not uncommon for a patient to succumb as the result of either perforation or hæmorrhage. On the other hand, the prolonged effect of the typhoid toxin on the heart and nervous system is quite sufficient to cause a fatal termination, and many patients die who present at the autopsy very trivial intestinal lesions (see Fig. 35).

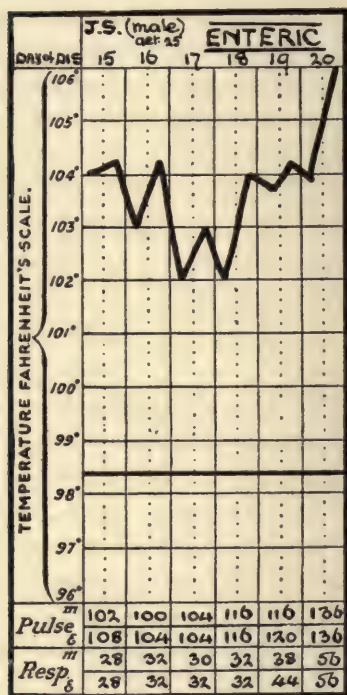


FIG. 35. A case of enteric fever fatal from toxæmia. There was considerable pulmonary congestion. Note the moderate pulse rate till a few days before death.

It must be understood that only a certain number of the patients, whose period of defervescence is delayed till the fourth or fifth week of the fever, present these grave symptoms. Sometimes, indeed, the illness may be extremely prolonged, and yet there may be no sign of the 'typhoid state'. Patients who have been appropriately treated from the early days of their fever are much less likely to suffer severely than those who have come late under observation. Occasionally the pyrexia and splenic enlargement are almost the only obvious signs of the disease.

Analysis of the Principal Features of the Period of Advance. *General appearance.* The face and expression of the patient are often characteristic, particularly in the second week. A slight, hectic-looking flush is often present on the cheeks, and the face is seldom congested or bloated. The conjunctivæ are lustrous, and the pupils somewhat more wide than normal. The expression

is suggestive of languor and apathy. If, however, the acute stage persists into the third week of illness, the flush on the face may become more marked and generally diffused. In bad cases the conjunctivæ are injected, and the pupils normal or actually small. In fact the general appearance approaches more to that which we are accustomed to associate with *typhus*.

The tongue, which in the first week has been covered with a somewhat creamy fur, becomes more dry, and is clean and red at the tip and edges. A small, triangular, clean, and glazed area is often noticed at the point

with the apex of the triangle directed up the tongue. As the fever progresses, the dorsum becomes yellow or brown, particularly in the centre, and the whole tongue becomes smaller in size. Later on, fissures, usually transverse, may appear on the surface, and these, if the toilet of the mouth is neglected, become covered with black crusts. Ultimately the tongue is red and glazed. Sordes is usually present on the lips and teeth, and occasionally there may be considerable faucial congestion. The breath is often very fetid.

The *abdomen* in the vast majority of cases is distinctly tumid. In many it is much distended. Tenderness is a frequent symptom, and this may be particularly localized in the right iliac fossa. Undue importance has been attached to the sensation of gurgling which may be obtained on pressure in this situation. Pain is occasionally complained of, and may be severe. The *spleen* is often readily palpable. It is always enlarged, though, when there is much tympanitic distension, it may be difficult to define it by percussion. Spontaneous rupture of this organ has been reported. Splenic tenderness is common.

The *eruption* is highly characteristic. On about the seventh day of illness, seldom before, the so-called 'lenticular' spots appear on the surface of the skin, the abdomen being the most usual situation. They are rose pink in colour, rounded in shape, and sufficiently raised above the surrounding skin-level to be appreciable when the finger is lightly drawn across them. If heavier pressure is applied, or if the skin is stretched, they temporarily disappear. In size they are small, seldom exceeding two lines in diameter. The life of each spot is from three to four days, but successive crops may appear daily, or at intervals, throughout the entire fever, even in early convalescence. Their first appearance, moreover, may be delayed till comparatively late in the illness. In many cases the eruption is extremely scanty, only two or three spots being visible on the body at any one time. More frequently as many as ten or twenty may be present, and occasionally they may be so numerous that hundreds can be seen at the same moment. When only few appear, they are usually situated on the abdomen, the flanks, and the lower part of the chest. They may also be visible on the back. But in profuse eruptions the whole trunk may be covered, and more rarely the extremities are also affected. In only one case have I seen a definite typhoid eruption invade the face. It is in such profuse rashes, especially if the case happens to be a severe one, that the spots are apt to lose their most valuable diagnostic feature, disappearance on pressure. Some staining of the skin occasionally occurs, and the typhus rash may be to some extent simulated, the spots being darker and sometimes almost

brownish in colour. Atypical spots are also not infrequently observed, a minute vesicle forming on the summit, and giving a more definitely raised or pimply sensation on palpation.

It is probable that, in most patients, spots appear at some time or other during the fever, but quite frequently they are absent when the case first comes under observation. Some writers state that an eruption is present in over 80 per cent. of typhoid patients, but this estimate is somewhat high, for hospital practice at least. As, however, many cases do not reach hospital till towards the end of the second week, it is extremely probable that spots may have been present, but have disappeared before admission. In patients of under ten years of age the eruption is not seen nearly so frequently as in older children and young adults, and, after thirty, spots are often absent. The profuseness of the eruption has not the same prognostic significance as that of typhus. On the other hand, it is frequently found wanting in mild and abortive cases.

Bacilli can usually be cultivated from the spots, which may possibly be due to inflammatory irritation caused by the lodgement, in the lymphatics of the skin papillæ, of small masses of agglutinated micro-organisms. It has been suggested that the preference shown for the abdomen may be explained by the nervous connexions of the skin in that situation with the foci of the disease in the intestine and spleen, and that some reflex action on the vaso-constrictors makes the retention of the clumps of bacilli more probable.

The stools are by no means always loose, but, when they are so, they usually assume the ochre yellow colour, which has caused them to be compared to pea-soup. They have a peculiarly fetid and suggestive odour. On standing in a glass jar, the stool forms two layers, yellowish and turbid supernatant fluid over a heavy deposit of particles of undigested food, curds of milk, epithelial débris, and shreds of separating sloughs. If hæmorrhage has occurred, the blood may be intimately mixed with the dejecta, giving them a dark colour, or clots of varying size may be seen in an otherwise typical stool. The reaction of the typhoid stool is alkaline. When the 'pea-soup' appearance is not present, the stools may be light in colour and pultaceous, or they may be dirty grey or occasionally dark green. They are seldom normally formed even in cases of constipation.

The temperature has been elsewhere considered. The *pulse* is of low tension, and often dicrotic. It may remain relatively slow throughout the whole duration of the fever, never perhaps exceeding 90, but more usually it has risen to 100 and over during the third week. In a severe attack it commonly exceeds 110, and in the worst cases may reach 130 or more. In

children and women it is often rapid throughout the whole illness. In older persons it may not attain its greatest rapidity till defervescence is well established. As to character, it is apt to lose its dirotism as the illness progresses, and it usually becomes much smaller as its frequency increases. Irregularity or intermittence is not common. The first sound of the *heart*, as heard at the base, is often very feeble ; sometimes, in severe cases, quite inaudible. Obvious dilatation is not usual. The feebleness of the heart is due to changes in the cardiac muscle as the result of prolonged toxæmia. Pericarditis and endocarditis are seldom observed.

As the disease advances the respiration is apt to be quickened, but seldom exceeds thirty to the minute in an adult, unless some pulmonary complication supervenes. A greater or less degree of bronchial catarrh is almost invariable, and is manifested by coughing, and by the presence of diffuse moist and dry sounds. Hypostatic congestion may be also regarded as a common condition in the more severe type of case, and is evidenced by cyanosis and by considerably accelerated respirations. It is not usually met with till the later stages of the fever (see Fig. 35).

The *nervous symptoms* of enteric fever are well marked. We have already noted the tendency for *headache* to appear early in the illness. It seldom, however, persists far into the second week, and usually disappears when the patient becomes delirious. *Insomnia* is often troublesome and persistent, unless treated early and effectively. *Delirium* occasionally assumes the maniacal type, the patient struggling to leave his bed and fighting with his attendants, but, by the time the third week is reached, the prostration is usually too great for these violent efforts, and the delirium is of the low muttering type commonly associated with the 'typhoid state'. Mental confusion is not uncommon and *deafness* is a very frequent symptom. Some patients are very drowsy and may be said to sleep through their entire illness. Children, however, who show this *somnolence* are apt to be extremely irritable and resistive when roused. Patients of this type often seem to object to light, and may constantly keep their heads under the blankets. In severe, and especially in sleepless, cases *subsultus* of the tendons is often present. More rarely the patient may pick at the bedclothes. Both retention and incontinence of urine and fæces are common.

The great *prostration* of the patient is shown by his helpless position on his back, and his inability to turn himself in bed, or even to retain himself on his side when turned. In the worst cases there is a tendency to slip down in bed.

When the head symptoms are well marked the case may bear a close

resemblance to one of meningitis. This is particularly the case in children, who occasionally present all the symptoms associated with that condition. Headache, vomiting, delirium, well-marked muscular rigidity, strabismus, and the 'tache cérébrale' may all be present. Twitching of the face and, more rarely, actual convulsions may also be observed. This symptom complex, sometimes described under the name of *meningism*, appears to depend purely on the toxins of the disease, and on no actual lesion of the brain surface. It is by no means incompatible with a complete recovery.

Attention has recently been directed to the *abdominal reflex*, which in most cases of typhoid is certainly absent during this period. I have, however, found it present throughout the fever in a fair number of patients.

The *urine* has the usual febrile characters. In the early stages of the illness it is often scanty and dark coloured. Towards the end of the period of advance, and throughout the stage of defervescence, the amount passed increases considerably and there is often actual polyuria. Traces of albumin are occasionally present, but large quantities are, in my experience, unusual. When the albuminuria is only slight, it no doubt results from the toxæmia. When larger amounts of albumin are present it is possible that there is some slight degree of nephritis. Seldom, however, is anything more observed than the presence of a few hyaline casts. Hæmaturia is extremely rare, nor are any of the other signs of a typical acute nephritis likely to be present. The amount of urea is much increased, chlorides are diminished, and it is not unusual to find indican in the urine. The diazo reaction of Ehrlich may be expected with some confidence from the sixth to the fourteenth days. Thereafter its presence is more uncertain. The method of performing this test, and its value in diagnosis, will be discussed on a subsequent page. The bacillus typhosus is often present in the urine, sometimes in such large numbers as to give a peculiar shimmering turbidity, when a specimen is held up to the light. Gwyn has reported that in one of his cases he estimated the number of micro-organisms at 500 millions per cubic centimetre. *Bacilluria* may be found quite independent of the presence of albumin in the urine. In a series of cases examined by Dods Brown at the City Hospital it was only associated with albuminuria in half of them. Pus in small amount may be also present, but there is not much clinical evidence of a true cystitis in these cases. As to the frequency of bacilluria, Dods Brown observed it in 53 per cent. of his patients, a somewhat higher percentage than that usually given. It seems to be most common in the later weeks of the fever and may persist indefinitely.

The *blood* is chiefly remarkable for its comparatively low leucocyte count, a feature which distinguishes enteric from other acute fevers. From 5,000

to 6,000 leucocytes is a very common figure, and definite leucopenia is frequently met with, the counts sometimes falling to 2,000, or less. It is unusual to obtain a count of more than 10,000, unless some inflammatory complication is present. The eosinophiles disappear and the polymorphonuclear cells are relatively and absolutely decreased in number, their percentage falling to 60 and under. Large mononuclears are relatively increased. The red corpuscles are much diminished, especially from the third week onward. The coagulability of the blood is lessened in the earlier stages, but much increased in convalescence. Bacilli can be cultivated from the blood in from 75 to 80 per cent. of cases during the first fortnight. Thereafter they can be recovered with much less certainty.

In addition to the characteristic roseolar eruption the *skin* presents few features of interest. In the second week, *sudamina*, tiny vesicles filled with clear fluid, are comparatively common. Occasionally more inflammatory-looking miliary rashes occur. Erythematous rashes are not infrequently seen, and that quite independent of *enemata*. They may be scarlatiniform, though punctation is not often very definite, or irregularly morbilliform in appearance. They probably depend on septic absorption from the bowel. Herpes, so common in pneumonia, is very rarely seen in enteric. The prolonged prostration makes bedsores extremely probable if the patient is not carefully nursed. A slight and almost imperceptible desquamation is often visible in convalescence.

Stage of defervescence. We have seen that the fall of the temperature is gradual. Signs of improvement in the patient's general condition are often slow in appearing. Sometimes, indeed, with the commencement of the lysis, a patient, who has previously been comparatively free from head symptoms, will suffer from increased confusion and delirium, and the urine and *fæces* may be passed involuntarily. In most cases, however, the worst symptoms gradually pass off, the tongue commences to clean, the abdomen loses its tumidity, and the spleen shows some decrease in size. Spots, however, may continue to appear on the abdomen, and the lysis is occasionally interrupted by well-marked rigors and even alarming rises of temperature. In most patients the appetite returns, and it is at this stage that the extraordinary hunger, so commonly seen in the convalescence of the disease, first manifests itself. The patient, under ordinary circumstances, still continues to lose weight. The duration of this stage varies with the time which the temperature takes to reach the normal line. From a week to a fortnight are the usual limits. Recrudescences of the pyrexia, however, or what may be fairly regarded as 'intercurrent relapses', may indefinitely prolong the fever.

Stage of convalescence. In favourable cases the temperature is from the first subnormal. Should it remain at, or slightly above, the normal line, there is always a greater probability of relapse. If, on the other hand, it be maintained steadily subnormal for ten days, convalescence may usually be regarded as established. The patient is extremely weak, but may feel reasonably well, and is always excessively hungry. Mentally he is often childish, and it is not unusual to see grown men behaving very much as might be expected of young children. The spleen, after a few days' subnormal temperature, is, as a general rule, no longer enlarged. The abdomen is soft, flat, and sometimes, after a prolonged fever, hollowed. The

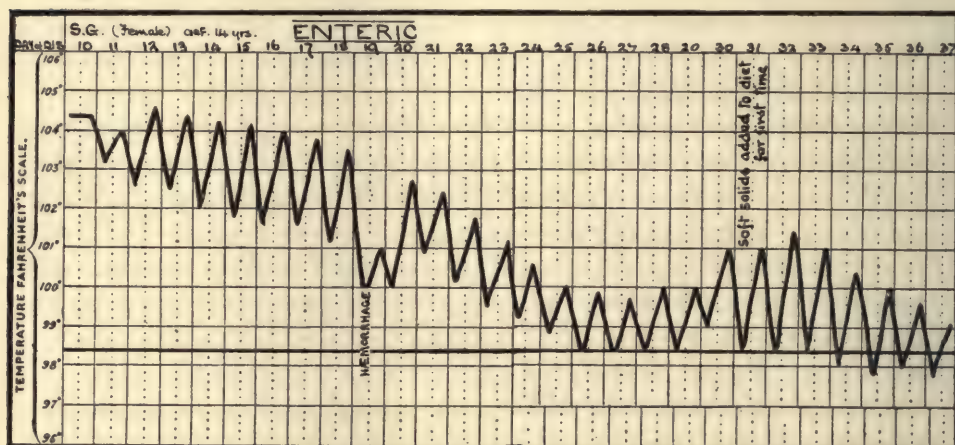


FIG. 36. A severe case of enteric fever. Note the effect on the temperature of a slight hæmorrhage, about 6 ounces, on the nineteenth day. The remitting temperature in convalescence was probably due to inanition, and subsided as the diet was gradually increased.

pulse gradually returns to the normal, but in some patients is liable to be extremely slow, and in a smaller number remains unduly fast. Recrudescences of fever, depending on causes other than typhoid infection, are very common. In some cases a temperature, normal in the morning and swinging up two or three degrees at night, appears to depend on inanition, and may be promptly checked by a suitable increase in the diet (see Fig. 36).

RESULTS OF TYPHOID ULCERATION. After the end of the second week of the illness there is always the possibility of the local condition in the gut adding to the risks which the patient is already encountering as the result of his toxæmia. The process of ulceration may cause either hæmorrhage or perforation, and I am accustomed to also associate with severe intestinal lesions such conditions as meteorism and dangerous diarrhœa.

Hæmorrhage. Intestinal bleeding occurring, as it sometimes does, in the first or second week of the fever, may be attributed to the rupture of capillaries in the Peyer's patches as the result of extreme congestion. I have not infrequently seen comparatively mild cases, admitted in the first ten days of their illness with a history of blood having been seen in the motions. This congestive hæmorrhage may be a counterpart to the epistaxis so frequently noticed at this period, and it is very seldom severe. Cases, nevertheless, have been reported in which, after death, the bowel was found to be full of blood and yet no necrotic changes had occurred. After the end of the second week, however, it is reasonable to suppose that the hæmorrhage is ulcerative in its origin, and that some small artery or vein has given way. The frequency with which this common complication of enteric fever occurs has been variously stated. Murchison, who excludes cases in which less than 6 ounces of blood were lost, gives the percentage of 3·77, and Goodall states that in 6·5 per cent. of his cases there was sufficient hæmorrhage to require treatment. In my own series of 1,700 patients, all cases of hæmorrhage being included whether slight or not, the complication occurred in 8·7 per cent. of the total number.

As is the case with perforation, men are more liable to suffer from hæmorrhage than women, my figures for the two sexes being 9·2 per cent. and 8·0 per cent. respectively, and in men the bleeding is, as a rule, more serious. As regards age, I have seen no case of hæmorrhage in children of under five years, and out of 511 patients below the age of ten, only three suffered from this complication. Between the ages of ten and fifteen the percentage incidence of hæmorrhage was four, but after fifteen years bleeding is much more common, occurring most frequently between the ages of twenty and thirty years.

The amount of blood passed may vary from one or two insignificant clots passed in an otherwise ordinary stool to an absolute gush of unmixed blood. In most cases, however, the quantity of hæmorrhage is something between these two extremes, and dark red or chocolate-coloured stools are passed, consisting of several ounces of blood with an admixture of faecal matter. Occasionally masses of almost black clots form the whole stool. An exact estimation of the amount of blood lost is a matter of considerable difficulty, as even one or two ounces make a most alarming show on a draw-sheet. When the hæmorrhage is very severe the bed-linen may be literally soaked. I remember in one case seeing the blood dripping on the floor through the mattress, and in another it trickled over the foot of the bed, the mattress in this latter instance being protected with a waterproof sheet. When such 'flooding' occurs, death may follow in a few minutes, and is seldom delayed

more than two or three hours. Complete recovery, however, is possible even after the loss of an astonishing amount of blood.

In the case of small hæmorrhages the first indication that bleeding has occurred is usually the presence of blood in the stool. Often, however, the temperature falls to a greater or less degree, the pulse usually increasing in frequency at the same time, and these signs may be observed before the hæmorrhagic motion is passed. If the bleeding is copious, the drop of the

temperature is usually well marked and is accompanied by other symptoms of collapse, such as a rapid feeble pulse and extreme pallor of the face. If the hæmorrhage is still more profuse, the temperature is subnormal, the pulse imperceptible, the respirations sighing, and the patient becomes anxious and restless and suffers from air hunger. If this stage of collapse is safely passed, the temperature regains its former level, often by the next day, as is seen in Fig. 36, or in more severe cases a day or two later, as is shown in Fig. 37.

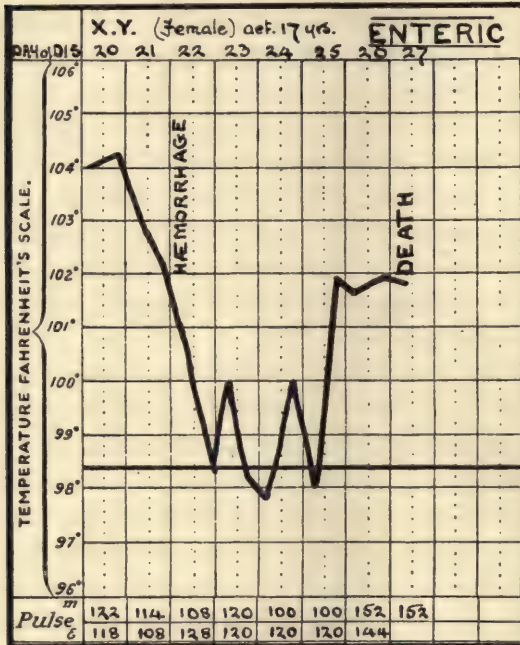


FIG. 37. Illustrating the continued depressing effect on the temperature of a profuse hæmorrhage. The bleeding was arrested, but death took place some days later as the result of exhaustion and toxæmia.

is probably most often seen when the original amount passed has not been very large. When, on the other hand, a patient has an extremely copious loss, it is not often repeated, the extreme feebleness of the circulation assisting to procure the natural arrest of the bleeding. Very troublesome and ominous cases are those in which small clots are passed daily in an otherwise typical typhoid stool. These may be the result of venous oozing from some damaged radicle, and, though the loss of blood is often trivial, patients suffering from this variety of hæmorrhage seldom do well. Many patients, again, may rally satisfactorily after a copious hæmorrhage, only

The hæmorrhage, when it has once occurred, may be repeated at comparatively frequent intervals, and this

to succumb to toxæmia some days later, their resistance having been, doubtless, lowered by loss of blood (see Fig. 37).

Perforation. This accident, the most dreaded of all the possibilities of enteric fever, is fortunately a comparatively rare occurrence, the proportion of cases being between 2 and 3 per cent., according to most writers, though Goodall reports as high a percentage as 4.9 in 2,482 patients. My own figures give 2.4 per cent. in a series of 1,700 cases, which, however, include a somewhat high proportion of children, in whom this complication is rare. As is the case with hæmorrhage, males suffer much more frequently than females, 3.4 per cent., as against 1.1 per cent., and the greatest percentage incidence occurs between the ages of fifteen and twenty-five years.

The common site for perforation to occur is the last 18 inches of the ileum above its junction with the cæcum, and, in most instances, it is within a few inches of the junction. But occasionally the upper part of the ileum, the appendix, or the large intestine may be perforated. The acuteness of the subsequent symptoms must to some extent depend upon the situation of the lesion. A perforation in the back of the cæcum, for instance, may give rise to a localized inflammation, and any spread to the rest of the peritoneum take place comparatively slowly, the general symptoms being correspondingly subacute. The most likely time for perforation to occur is towards the end of the third week or later. Cases have been reported as occurring in early convalescence and in relapse, but these must be unusual. I have never seen an instance of perforation in a relapse, and only one case (not one in this particular series) after the temperature had become normal.

The accident has been attributed to various causes, such as the taking of solid food, straining at stool, or incautious handling by the nurse or medical attendant, but there was no obvious reason for perforation in any of my own cases. It seems more reasonable to regard it as due to a deeply extending necrosis of the lymphoid tissue and subjacent structures, and the subsequent detachment of sloughs. Sometimes a suggestive warning of possible perforation is given by slight abdominal pain, apparently due to local peritonitis over the thinning base of the ulcer. Such pre-perforative pain may last for two or three days before the accident happens, or, again, after pain, apparently of this nature, perforation may fail to occur. Not infrequently the temperature remissions are less well marked for two or three days before the bowel gives way, and the same may be noticed before a hæmorrhage, a 'straight line' temperature probably being often associated with conditions of deep ulceration. But little dependence can be placed on these points. Occasionally the accident happens in comparatively mild cases with good morning remissions and a slow and steady pulse. And in

some ambulatory cases its occurrence has been the first sign of the existence of the fever itself.

The most common and most striking symptom of the complication is *pain*, which is often sudden and violent in its character. One of my patients wakened suddenly from a quiet sleep with a cry, and explained to me that he was dreaming that he had been kicked savagely by a horse. A few hours later he was operated on, unfortunately without success. And many cases show as sudden and unexpected signs of the accident having occurred. In others, however, the pain is more moderate in character, and develops more gradually, and in some there is little or no complaint of pain at all. It is obvious that the amount of toxæmia, from which the patient happens to be suffering at the moment, modifies considerably the character of the symptoms. A man in the 'typhoid state', with his senses dulled, and perhaps almost comatose, is not likely to adequately express what he feels, if, indeed, he has much feeling left. We will expect to get the clearest indications in patients who have been comparatively well up to the moment of perforation. Cases, again, in which there has been much meteorism and perhaps some pain and tenderness for some days previously, will present much less striking features than those in which the abdomen has been merely slightly tumid.

In a fair number of patients, particularly in those who have suffered from sudden and violent pain, there may be a marked fall of *temperature*, and considerable collapse. In such cases the pulse rapidity is much increased (see Fig. 38). But this drop in the temperature must not be counted on; in a considerable number of patients it is altogether wanting. In a few, if the temperature moves, it is in an upward direction. It is rare, however, for the pulse-rate not to be affected. Other early symptoms may be *shivering*, which is highly suggestive, but which is often absent, and the passage of one or two loose motions, which, in patients who have not previously suffered from diarrhœa, may be worth considering, together with other more important points, in a doubtful case. In many patients the face may express *anxiety* from the first. Vomiting may occur at once, but is usually delayed till peritonitis is established.

There is little to be gained by attempting to localize the pain. All parts of the abdomen may be complained of, and it is not unlikely that the patient will refer the pain to his epigastrium. But localized *tenderness* may be discovered, often in the right iliac fossa. The abdomen, in many cases, presents a great change in appearance from the last time on which it was examined, though in patients who have previously suffered from meteorism such alteration may not be noticed. In the great majority of cases the abdomen

does not move on respiration, or at best moves extremely slightly. On palpation, in addition to the tenderness usually present, there is a sensation of resistance owing to the patient holding his abdominal muscles. This will sometimes be found to be only unilateral. In well-marked cases the liver dullness in the nipple line is completely obliterated or much encroached upon. Occasionally, however, this sign takes some hours to develop.

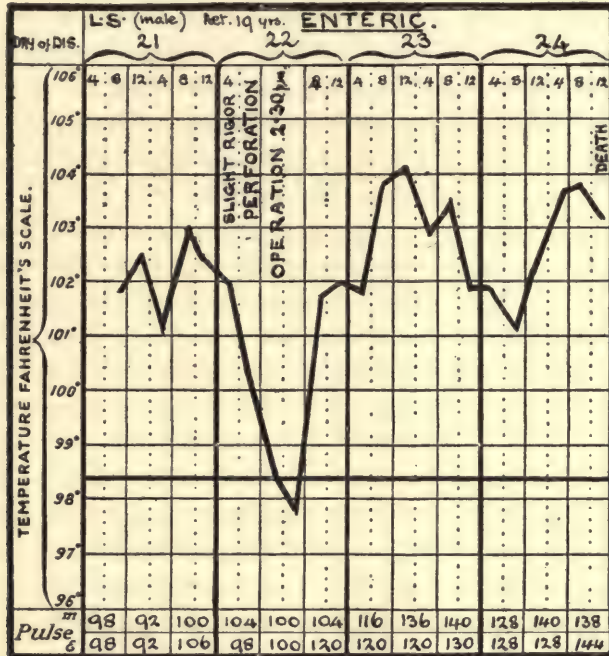


FIG. 38. Showing the four-hourly temperature of a patient who suffered from perforation on the twenty-second day of an attack of enteric fever. The symptoms first noted were a slight rigor and a fall of temperature. Abdominal distension followed operation. No subsequent peritonitis, but death from toxæmia.

In a few hours, if the case is left untreated, *vomiting* usually sets in, suggesting the onset of peritonitis. The abdomen becomes larger, more generally tender, and more resistant. It is sometimes enormously distended, with glistening stretched skin. The patient does all he can to spare the movements of his abdomen, and lies with his knees drawn up to relax his muscles. His face becomes pinched, and is pale or livid. His anxiety is obvious, and, unfortunately, his consciousness is usually acute. The temperature, if it has not previously fallen, now tends to do so, and in many cases the pyrexia from the time of perforation to the fatal termination is very inconsiderable. Just before death it may rise to comparatively high levels, or,

on the other hand, the patient may die with a subnormal temperature. The pulse is irregular, thready, and very rapid. Towards the end it may be quite imperceptible. Death usually occurs within three days, but Osler has reported cases in which the patient lingered for over a week. In these circumstances it is reasonable to believe that the perforative peritonitis has at first been shut off in some way or other from the general cavity of the peritoneum. It is said that some patients recover without operation from this dreaded complication. I should say that such a result must be extremely rare. It is well known that the abdomen has been frequently opened for perforations which did not exist. Such cases, recovering without operation, would doubtless be regarded as instances of cure. It is safer to assume that the condition, unless surgically treated, is a hopeless one, and this emphasizes the necessity for prompt and accurate diagnosis.

It will be convenient to consider the main points in the *diagnosis* here. It will be easy in proportion to the mildness of the toxic symptoms previously exhibited by the patient. When toxæmia is severe the senses are much blunted, and it may be that even such a cardinal sign as pain will be wanting. It is, further, more difficult to appreciate the presence of tenderness in these circumstances.

Pain, then, appearing suddenly in a patient who previously has not complained of it, should always be regarded with the greatest suspicion, and instructions should be left with the nurse that its occurrence should be reported without delay. If, as sometimes happens, collapse and a rising pulse-rate accompany the onset of the pain, the indication is fairly clear, but it must be remembered that this cannot be expected to happen frequently. As regards the examination of the abdomen I am inclined to look first to see if it moves on respiration. If comparatively free movement is observed, the idea of perforation, so far as my experience goes, may be discarded. If the breathing is entirely thoracic, or if only slight movement of the abdomen is perceptible, further examination is necessary. Rigidity of the abdominal muscles is a most important sign, and this, taken together with tenderness and an immobile abdomen, would justify operation. Obliteration, or marked diminution, of the liver dullness is also a very valuable, if not absolutely trustworthy, sign. Sudden, if only slight, changes in the appearance and feel of the abdomen, when compared with the last time it was examined, should make the medical attendant think of the possibility of perforation, and these will not be appreciated unless the abdomen is examined daily throughout the fever as a routine. In toxic cases such changes may be the only indication that an accident has occurred. In less poisoned patients, anxiety and the gradual assumption of the

abdominal facies are points of importance. An initial shiver, which, however, has been computed as occurring in less than 20 per cent. of the cases, would also suggest perforation.

As regards the information to be obtained from a blood count, opinions differ considerably, but the absence of leucocytosis, rather than its presence, appears to be most suggestive. That is to say that if, immediately after the accident is suspected to have occurred, the count is low, there is certainly a strong presumption against perforation. A little later, however, when peritonitis is fully established, low counts are not uncommon. A high count, on the other hand, is liable to be found in many of the conditions sometimes mistaken for perforation. In any case blood examinations in an emergency are of only modified value, unless the leucocytes have been systematically counted at frequent intervals throughout the fever, and are often out of the question in private practice.

It must never be forgotten, while any given case is under consideration, that perforation is imitated by a number of other conditions. Several cases of my own I am quite unable to explain. They suffered from sudden pain, tenderness, some resistance, and in one instance a fall of temperature, but the abdomen was never absolutely immobile and the face never looked quite typical. Vomiting was a prominent symptom in some of these patients, who all ultimately made good recoveries. What was responsible for the mimicry of perforation in these cases was never satisfactorily proved, but after each of my almost hourly visits to them I expected to have to recommend operation at the next.

It will be well to mention here some of the conditions that must be excluded. Cystitis due to retention of urine should be thought of, but is not likely to occur in a well-managed case. Pain, accompanying a concealed hæmorrhage, may suggest that the more fatal complication is present. Patients suffering from pneumonia, starting perhaps with diaphragmatic pleurisy, have been operated on for perforation. Cholecystitis has been responsible for operative interference, as has also thrombosis of the iliac vein. Gastritis, enterocolitis, and appendicitis have been also among the conditions subjected to an exploratory operation, and a case has been reported in which scybalous masses of fæces were all that was found to account for the symptoms. Colic, due to such a cause, may be excluded, Goodall points out, by watching for peristaltic action, which, if visible, contradicts the possibility of perforation, paralysis of the gut being an early symptom.

The management of a case of perforation, once it is diagnosed, will be discussed under the head of treatment. But it is not out of place here to lay down as a golden rule, *once perforation is suspected never give*

opium, as to do so will often deprive us of our best chances of coming to a diagnosis.

Diarrhœa. As has been said above, this condition is often associated with extensive ulceration. Three or four loose motions in the day need not be regarded as anything very serious, but a greater number often cause an undesirable amount of exhaustion. They are also a great source of worry and anxiety to the patient and may seriously disturb his night's rest. Tenesmus is seldom present unless hæmorrhoids or some other rectal or anal condition complicates the case. Occasionally, however, very small involuntary evacuations, merely a dribble of fæcal matter, are passed at very frequent intervals, and these do much to wear the patient out, the constant attention of the nurses and the changing of the draw-sheets being often fatiguing. Fortunately few patients who are judiciously dieted suffer much from diarrhœa in the strict sense of the word.

Meteorism is also apt to be associated with deep ulceration and the presence of putrefying matter in the intestine. Like diarrhœa, it seldom occurs in well-managed cases which come early under observation, but, when present, it is often extremely dangerous. The abdomen may be literally ballooned and extremely tense, and in a few of my patients the condition was so intractable that it ultimately killed them by embarrassing the action of the heart. It is also probable that it increases the likelihood of perforation. Paresis of the gut with intense meteorism was responsible for the death of one of our operative cases which had presented every sign of doing well. The abdomen may be very large, however, and somewhat tense, without any particular danger to the patient.

RELAPSE. Few acute diseases have a more decided tendency to relapse than has enteric fever. The explanation of this peculiarity is not at all easy, and various theories are held on this subject. The view of Durham, that various strains of allied bacilli may be concerned in the original infection, and that the bacilli of one particular strain may only have the chance of exercising their influence after the original fever is over, is as convincing as any, but so far lacks bacteriological proof. It can be readily conceived that immunity might be acquired only against the strain of micro-organisms predominating in the primary attack, and that other strains issuing from the spleen or other organs might be capable of producing a reinfection. If we do not accept this view, we cannot regard the serum reaction as a sign of immunity, for the reaction is often strongly positive when the relapse occurs. Widal, however, only claimed that the reaction was a test of infection.

It is commonly held that indiscretions in diet are frequently responsible

for relapses. In my own experience, while indefinite pyrexia, with no symptoms of enteric fever, often follows an addition to the diet, true relapse seldom does so, but seems altogether independent of this cause, occurring indeed with the greatest frequency in cases somewhat rigidly dieted.

A relapse is a repetition of the original fever, usually, but not always, in a shorter and milder form. It should bear sufficient resemblance to an ordinary attack of enteric fever to be recognizable as that disease, and it is this character which distinguishes it from febrile disturbance in convalescence due to other causes. It is usual to restrict the term to those cases in which, after an apyrexial interval of longer or shorter duration, the fever is once more repeated, but those exacerbations of temperature, with a return of acute symptoms, which occasionally interrupt the period of defervescence of the original fever, and which have been called *intercurrent relapses*, are obviously due to the same pathological conditions as is the true relapse. The apyrexial interval may be quite short, perhaps only twenty-four hours, is often about a week, and seldom exceeds a fortnight, though instances of relapse after five weeks have been reported, and in one case of my own the interval was nearly four. During this apyrexial period it is not uncommon to see the temperature normal, rather than at the distinctly subnormal level usually met with. Even if it is subnormal in the first days of convalescence, it frequently shows a tendency to oscillate up to, and above, the normal line for three or four days before the relapse declares itself. It is usual, moreover, to notice that the spleen remains large during this stage, instead of resuming its natural size rapidly, as we would expect in a more favourable case. The splenic enlargement certainly suggests that it is to bacilli harboured in that organ that the relapse is in reality due.

The invasion stage of the relapse is hardly so insidious as that of the original attack, the acme in many cases being reached in three days, while in some it is attained in a few hours. Except in the last instance, however, the rise of temperature is similar in its step-like gradations to that of the primary fever. The diazo reaction usually appears early in the urine, being seldom absent after the third day. The roseolar eruption also appears somewhat early. The abdomen once more becomes tumid, and the abdominal reflex, usually active in the apyrexial interval, is again abolished. Any of the features of the original attack may be reproduced, but my experience has been that ulcerative complications are rare, the short duration of most relapses being no doubt against their development. The average duration, indeed, can hardly be more than from ten days to a fortnight, and sometimes the whole process is completed within a week.

Severe relapses, however, are sometimes met with, more especially if the original fever has been of less than average severity. Of fifty-three cases, reported by Murchison, seven terminated fatally, perforation being the cause of death in two instances. On the other hand, I only saw two deaths in the ninety-five relapses which occurred in my series, and in one of these cases hæmorrhage caused the fatal result.

As regards the frequency of relapse, the percentage incidence was 5·5 for the 1,700 cases, but in some outbreaks there appears to be a greater tendency for the fever to repeat itself, and for one year my percentage was as high as 13 per cent. Intercurrent relapses, it may be noted, are not

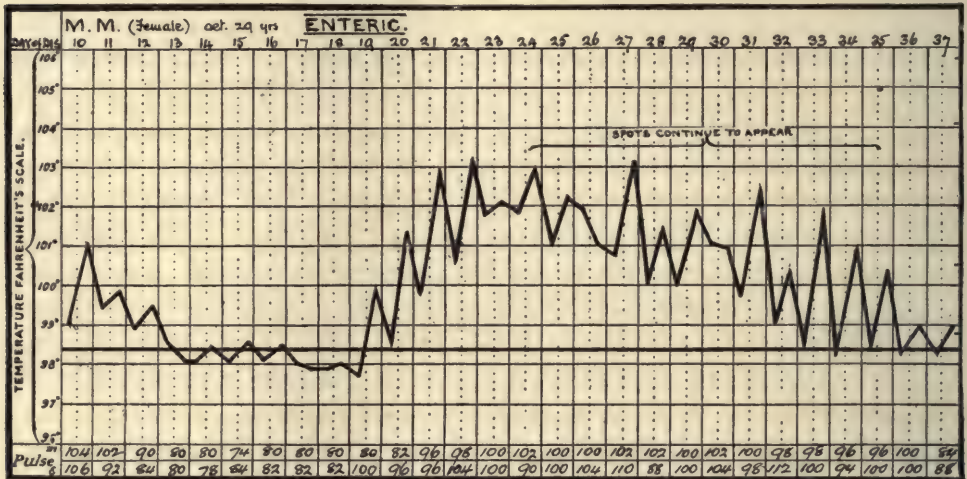


FIG. 39. Illustrating relapse after a short abortive fever. The relapse was moderately severe and lasted nineteen days. The relapse, in a milder form, was repeated a month after its commencement. The onset in each case corresponded with the time at which a menstrual period was expected.

included in these estimates. Females suffer more frequently than males, 7·0 per cent. as against 4·3 per cent., and, if the age period between fifteen and forty-five years is alone considered, this difference is accentuated, the figures being 9·2 per cent. and 4·9 per cent. respectively. This is to some extent explained by the frequency with which a relapse starts at a menstrual period, whether the actual flow is present or not. It is not unusual to see relapses repeated at monthly intervals in women, who may have four or five attacks of the fever before convalescence is thoroughly established. However, three relapses are very rarely exceeded. Presumably the resistance to reinfection is lowered at the menstrual epoch. The charts (Figs. 39, 44) show a relapse starting with menstruation. I have only seen one instance

of relapse in a child of under five years of age, but in the succeeding quinquennial period it is as common as later in life. It has been stated that systematic treatment by the cold bath method increases the liability to relapse. Genuine *second attacks* doubtless occur, but in many cases may be due to infection with a different micro-organism to that of the original attack.

Post-typhoid pyrexia. From relapse must be distinguished those rises of temperature which so frequently interrupt the convalescent stage. These have been called 'recrudescences', but as this term has been also employed to designate 'intercurrent relapses' it is perhaps well not to make use of it. The temperature in convalescence is extremely mobile, and is often raised considerably by even a slight degree of constipation, or an apparently insignificant addition to the amount of food allowed. Starvation again is sometimes the cause of a high swinging pyrexia, and the various sequelæ of enteric fever are also responsible for temperature elevations at this period. These febrile attacks are seldom prolonged, and quickly subside when the cause is adequately dealt with. None of the classical symptoms of the original fever are repeated during their course. The diazo reaction does not appear in the urine, and the spleen is not particularly enlarged.

VARIETIES OF ENTERIC FEVER. 1. Mild forms. The three-week type of enteric fever, which is so frequently met with, may be fairly classed as one of the milder forms of the disease. The lysis in these cases does not begin later than the end of the second week, and it is very questionable if ulceration occurs. Of still shorter duration is the *abortive* type, which may last from ten days to a fortnight, and which is illustrated by the original fever on the chart (Fig. 39) of the relapsing case, and also by the chart annexed (Fig. 40). The symptoms in such cases are often so mild that it is only by the aid of the serum reaction, and from the fact that other members of the same family may be suffering from typical attacks, that they can be recognized as enteric fever. But occasionally the onset and the invasion symptoms may be extremely well marked. It is perhaps not strictly logical to include *ambulatory* cases under the mild forms of the disease, for it is well known that deep ulceration may occur in these cases, and that the first obvious sign of the illness may be a fatal hæmorrhage or perforation. The fever appears to run its usual course, but, except for a general sensation of malaise, the patient may remain comparatively well and continue his work. Usually he ends by becoming acutely ill, and some of my most fatal cases have been those in which the patient was able to keep his feet with comparatively little inconvenience till the end of the third week.

2. **Severe forms.** In most cases of enteric fever which exceed three weeks' duration the temperature has reached the normal by the end of four weeks, and this may be held to be the average type. But prolonged forms exist in which the period of advance may continue for even as long as six or seven weeks, the complete duration of the fever being from eight to ten. Such prolonged toxæmia causes great prostration, and, as severe ulcerative changes may also be present in this type of the disease, the danger to the patient is very great. In other cases, again, the length of

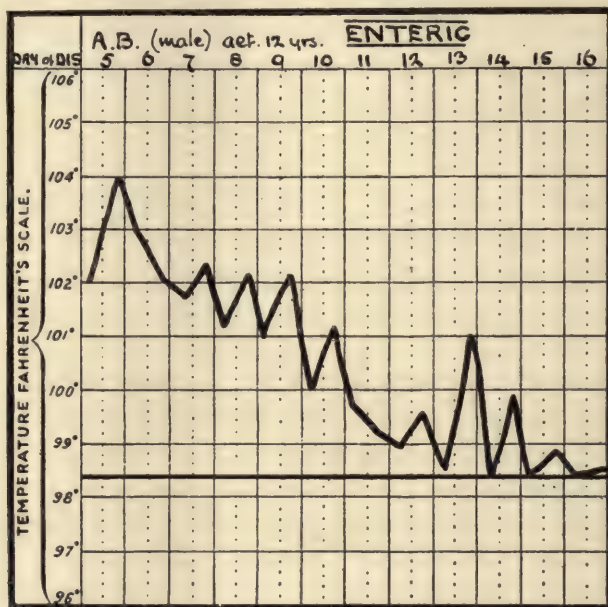


FIG. 40. An abortive case showing decline in the temperature from the sixth day, and completed in just over a fortnight. Other members of the same family had more prolonged attacks.

the fever may not exceed the average, but the ataxic or adynamic symptoms may be unduly accentuated, owing either to special susceptibility on the part of the patient or to a particularly virulent infection. The temperature in such cases may often exceed the average, and the morning remissions may be exceedingly slight. The pulse also is usually rapid, seldom falling below 120 per minute, and pulmonary congestion is common. As is the case with most of the acute infections, there is a *hæmorrhagic* type of enteric, which is, fortunately, most uncommon. The only case I have seen was shown me at the Aberdeen City Hospital by Dr. Banks. The patient, in addition to purpuric hæmorrhages in the skin, suffered from profuse epistaxis and

hæmaturia. The condition seems to be relatively more frequent in children and is very fatal. Some patients, without actually assuming this type of the fever, are apt to bleed much from the nose and gums, and in one of my cases death occurred shortly after a copious hæmorrhage from the nose.

3. **Apyrexial typhoid.** In this most interesting variety of the fever all the classical symptoms are present except pyrexia. The illness is not by any means trivial. In two of the four cases which have come under my own observation it was, if anything, more than averagely severe. The patient

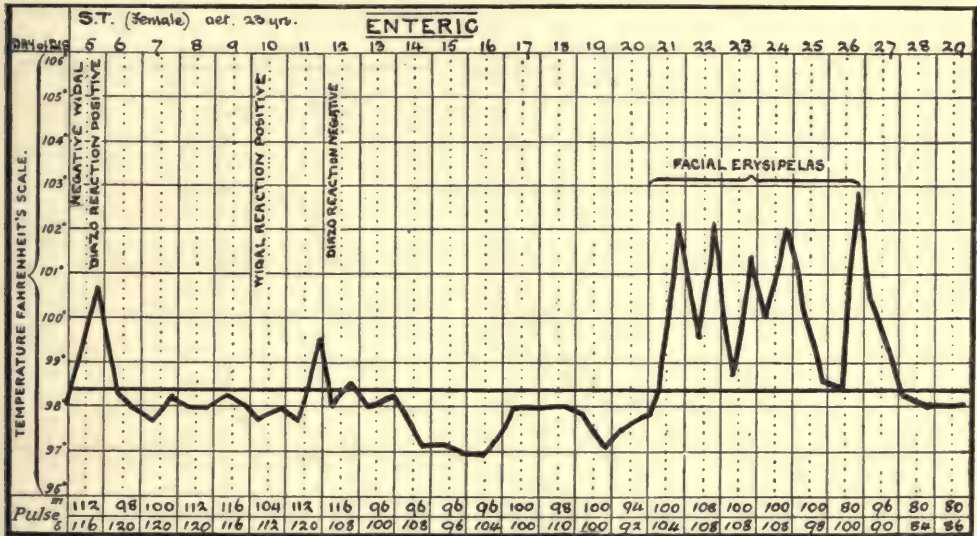


FIG. 41. A case of enteric fever from the fifth day, running an apyrexial course. Typical appearance, wasting, ochre stools, and tumid abdomen. Positive Widal reaction. Diazo reaction brilliant from fifth to eleventh days. Note rapid pulse. Diarrhœa well marked for the first fortnight. Complicated by facial erysipelas.

undoubtedly suffers from 'fever' though the temperature is not raised, and wasting is as prominent a feature as in the ordinary attack. Of my four cases it was the original fever in three patients and a relapse in the other which exhibited this eccentricity of type. Two charts are annexed (Figs. 41 and 42). It will be noticed that, in the first, some fever was probably present at the time of onset, and it is reasonable to assume that it was well marked; otherwise the case would hardly have reached hospital on the fifth day. From that day onwards the temperature remained normal, the pulse, however, being much accelerated, especially if the absence of pyrexia is considered. Diarrhœa, or numerous loose motions of a typical appearance, was present throughout the illness, the abdomen was tumid, and the spleen

enlarged. The patient was flushed, prostrated, and looked extremely ill. The diazo and serum reactions appeared much as would be expected in an ordinary case. There was no roseolar eruption. The temperature ultimately rose, as the result of an attack of facial erysipelas, and this febrile reaction appeared to do good as, by the time it subsided, convalescence commenced. In the second case the relapse commenced in the usual manner, but the pyrexia only lasted three days. Thereafter the temperature seldom exceeded the normal line. Spots and other diagnostic symptoms were present. In a third patient there was well-marked fever at the onset, accompanied by so much pain that she was operated on for appendicitis. The operation,

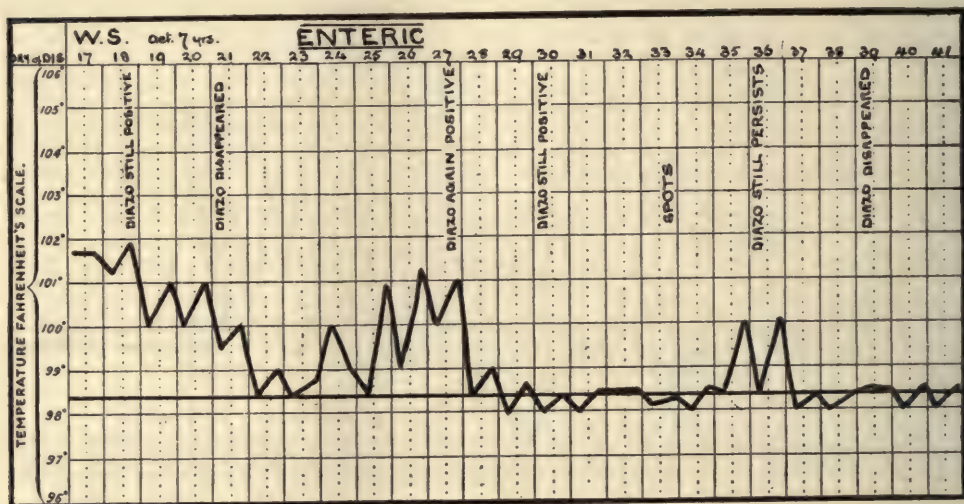


FIG. 42. Showing an apyrexial relapse, lasting from the twenty-third to the forty-first day, and accompanied by all the signs of fever (except pyrexia)—a tumid abdomen, palpable spleen, roseolar eruption, and diazo reaction.

however, made the diagnosis clear, and she was notified as enteric fever. The temperature was high at the moment of her admission on the seventh day of her illness, but thereafter was quite normal, although as regards her other symptoms the illness continued for a fortnight longer. Whether this change to apyrexia was caused by the operation or not it is difficult to say.

The cases are interesting as showing that a diagnosis of enteric fever must not be dismissed on account of a normal temperature. The type does not appear to be very uncommon. Curschmann reported several instances of it, and it has also been described by Osler and others. It is, however, very liable to pass unrecognized.

4. **Enteric fever in children.** The disease is rare in infancy, though a case at the age of three weeks has been reported. In my series no patients were under one year of age, and only nine were under two. After three years of age, however, the disease is relatively common, as will be noticed in the table on page 326. It is, on the whole, milder in children of under ten than in older persons, but severe cases are not infrequently met with, death in most cases resulting from toxæmia, rather than from ulcerative complications. The latter, indeed, are distinctly rare, only three of my 511 cases under ten years of age suffering from hæmorrhage, while five died as the result of perforation. Meningism is often well marked,

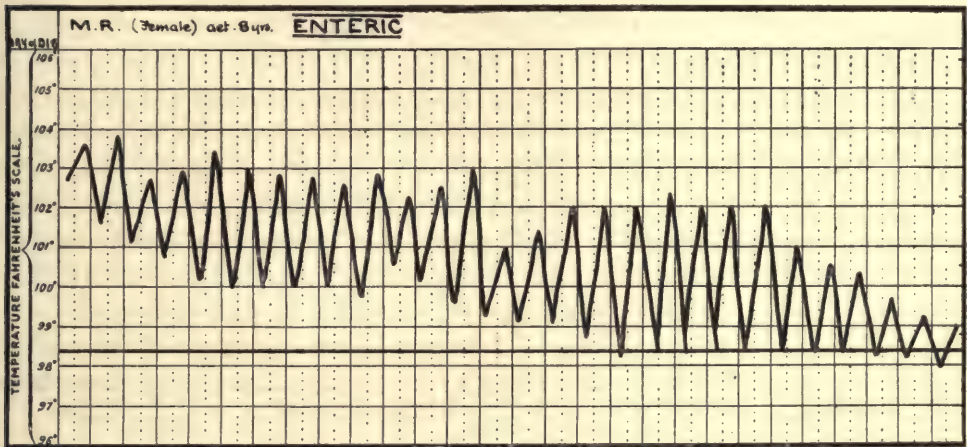


FIG. 43. Enteric fever in a child, illustrating the 'infantile remittent' type of temperature.

and it is in patients of this age that the difficulty in differentiating the disease from tubercular meningitis usually occurs. Many children show a great objection to light, and are inclined to lie with the head covered with the bedclothes, and they are also apt to be exceedingly irritable when touched. The temperature is often high, particularly in the early stages of the fever, but it is in most instances characterized by very decided morning remissions, a peculiarity to which the old name, 'infantile remittent fever', is doubtless due. The pulse does not show the same comparative slowness as in older persons. Spots are less frequently noticed than they are in adults, and this is especially the case with patients under five years of age. Enlargement of the spleen is pronounced, and the organ is usually palpable. Diarrhœa is relatively common. Such sequelæ as otitis media and superficial skin abscesses are often seen in prolonged cases, and I have seen two instances of cancrum oris. My statistics, however, do not include

a case of venous thrombosis occurring in a child of under ten. Next to the meningeal conditions, the diseases most likely to be confused with enteric fever at this early age are broncho-pneumonia and gastro-enteritis.

5. Enteric fever in the aged. While the disease is comparatively rare after forty, well-marked cases have been described in persons as old as seventy or eighty. Only three of my patients, however, were above sixty years of age. The fever tends to be of an adynamic type, and the temperature is often subacute. The illness is apt to be protracted, and death from exhaustion and cardiac failure is to be feared.

6. Complicated types. Types of the fever in which from the first the symptoms appear to point to localization in some particular organ, such as the lung, the kidney, or the meninges, will be noticed under the complications of the disease.

THE PARATYPHOID FEVERS. It has been suggested above that it seems more convenient to regard these fevers as subvarieties of one clinical, if not bacteriological, entity, enteric fever. It must, of course, never be forgotten that the three varieties are absolutely distinct in so far that they confer no protection against each other. It is true, also, that the paratyphoid micro-organisms have been associated in many instances with the production of symptoms more suggestive of acute food-poisoning than of enteric fever, but in this connexion it is well to remember that the bacillus enteritidis only differs from the B bacillus in its agglutinating properties, and that the differentiation of the micro-organisms may not in all cases have been clear. Paratyphoid fever has been rare in Great Britain and France, and its appearance in the early days of the war has been attributed to importation by troops from the East. We have been accustomed to associate the A variety with India, and the few cases which have been seen in Britain appear generally to have been due to the B type. In Edinburgh, although we have been on the watch for paratyphoid infections for many years, only stray cases have been identified, and so far as I am aware I have included none in the series of 1,700 cases of enteric fever on which my experience is based. But last year the majority of our cases were paratyphoid B, and it seems clear that this infection has been introduced by carriers from the different theatres of war. While my experience of this type has been a comparatively small one, a little less than fifty cases, it has been quite extensive enough to make me doubt the clinical distinctions made by many authors between the different types. Hæmorrhage has been frequent, phlebitis perhaps unduly common, and the duration and severity of the attacks have been quite up to the average. There has been nothing in these cases to distinguish them from the typhoid bacillus infections lying beside them

It is interesting indeed to read the extremely contradictory reports of the presence or absence of a particular symptom in paratyphoid fever as collected by Vincent and Muratet. One observer says spots do not occur, another that they are unusually frequent and numerous; some state that nervous symptoms are more common, others that they are absent or ill marked. It really comes to this, that, like the true typhoid infection, the paratyphoid varies very much in its severity and its symptomatology, and that probably the most that we can do clinically is to make a guess as to which micro-organism is responsible, just as I have been able in the past to associate a particular case of enteric fever with a particular source of infection because its symptoms conformed more to those of cases from that source than to those of other individuals infected elsewhere.

But while it is undoubtedly the case that all the severe complications of 'typhoid' fever may occur in the paratyphoid varieties, and that hæmorrhage, perforation, meningitis, phlebitis, 'paratyphoid spine', and relapse are all met with, it appears to be generally agreed that the case mortality is lower. But even as regards this point Goodall very justly reminds us that 'different laboratory methods in different hands will yield different results'. During the same Belgian epidemic the fatality rates at two hospitals were, at the first, typhoid, 9·7 per cent., paratyphoid, 19·2 per cent.; at the second, typhoid, 20·9 per cent., paratyphoid, 2·1 per cent. Figures like these suggest that laboratory findings are not always above suspicion.

The incubation period of the paratyphoid fevers is stated to be from nine to fifteen days. The onset is usually more abrupt and is more frequently attended by shivering. The pyrexia reaches the acme more rapidly. Constipation is common, but diarrhœa may be present and may in some cases be noted before the commencement of the attack. The duration of the fever tends to be shorter than that of typhoid, but relapses are at least as frequent. In my own experience I have found the diazo reaction occurs as in the ordinary fever. The only conclusion is that bacteriological means are necessary to make a diagnosis and cannot be dispensed with if specific therapy is to be attempted.

COMPLICATIONS AND SEQUELÆ. Only those conditions which are met with comparatively frequently in the course and convalescence of the fever need be considered. It will be sufficient to mention the others. Perhaps the most common is **thrombosis** of the veins, which may be expected to declare itself either in the period of defervescence or during the convalescent stage. In some cases complete thrombosis does not appear to be present, but an acute phlebitis occurs with marked tenderness over the line of the affected vein and only moderate œdema. The complication was noticed

in a little over 2 per cent. of my series of cases, and in every instance the patient made a good recovery. This is the termination which we would naturally expect, as, except for the somewhat remote possibility of the detachment of the thrombus, the only risk attached to the condition is the gangrene which, in rare instances, follows it. The veins affected are nearly always those of the lower extremities, but in one of my cases the scrotal veins were alone implicated. Of the extremities, the left is much more frequently affected than the right, twenty-three to ten of my cases. Of the veins, the femoral, the internal saphenous, and the popliteal are most often thrombosed. The symptoms usually commence with some suddenness. Acute pain in the affected limb is complained of, and the temperature rises quickly. Occasionally a rigor may mark the onset. The pyrexia, while it lasts, is often of the 'spiking' variety. The leg is very much swollen, though the œdema is seldom so well marked as in cases of phlegmasia alba dolens following delivery. The most likely time for the complication to make its appearance is within a fortnight of the temperature attaining the normal line, but in some of my cases it interrupted the stage of defervescence.

The bacillus typhosus has been isolated from the thrombi and from the vessel walls, and the lining endothelium has been found to be destroyed at the situation of the clot. Some local damage of this nature may determine the commencement of coagulation at a particular point. We have seen that during enteric fever the blood coagulates less readily than in health, but Wright has pointed out that the contrary is the case in convalescence, and that the blood is extremely coagulable. This he attributes to the excess of calcium salts taken in by the patient who has for long been kept upon an exclusive milk diet. I have, personally, always been inclined to believe that thrombosis is most likely to appear in patients who have been under-stimulated, but I can adduce no definite evidence in support of this view. As regards the frequency with which the veins of the left lower extremity are implicated, Keen adopts the explanation that the left iliac vein is to a certain extent pressed on by the left common iliac artery, and that this is sufficient to determine the occurrence of the thrombosis on that side. Goodall holds that the overloaded rectum of the patient in convalescence, a period at which constipation is common, exercises a similar influence. Possibly both causes play some part in the production of the condition.

Arterial thrombosis is happily much more rare than that seen in the veins. It may be due either to embolism, or to an obliterating arteritis which itself may depend on the action of the bacillus. The one case which has come under my notice declared itself so suddenly that we attributed

it to embolism, although no heart lesion was definitely recognized. The vessel blocked was the left femoral artery. Collateral circulation was fortunately established, and the dry gangrene, which so often follows this condition, did not result. The symptoms of this form of thrombosis are cessation of pulsation in the branches of the affected artery, and coldness of the limb as compared to the other side. There is considerable pain and some swelling.

A comparatively common complication of enteric fever is *lobar pneumonia*. It was noted as present in nearly 2 per cent. of my 1,700 cases. It may either occur as an intercurrent complication during the course of the fever or it may initiate the attack, masking more or less completely the usual symptoms of the onset. In the first case, while it may complicate any stage of the illness, it is perhaps most commonly seen at the end of the second week. The pneumococcus is usually present in the sputum and is, doubtless, the exciting micro-organism. The onset is not always very obvious. There may be pain in the side, and perhaps even a rigor, but in the great majority of cases the first suggestion of the presence of the complication is an acceleration of the respiration. Sputum is often wanting altogether, and cough may be very slight. It is only by examination of the chest that diagnosis can be made. In one or two of these cases I have seen a definite crisis show through the typhoid pyrexia, the temperature rising immediately afterwards and continuing its ordinary course. The restriction of the inflammatory process to the limits of a lobe, its usually unilateral position if the base is affected, and the characteristic signs on auscultation serve to distinguish a complicating pneumonia from the hypostatic condition so frequently observed, in which defective resonance at both bases and feeble breath sounds are the most prominent features.

When, on the other hand, the fever starts abruptly with all the symptoms of an acute pneumonia, we have the condition known as **pneumo-typhoid**. The classical symptoms of pneumonia being obvious, the fact that enteric fever is also present is apt to be missed, and it is only when the crisis fails to make its appearance, and the whole type of the illness changes during the second week, that the true nature of the condition is realized. The typhoid bacillus may be present in the sputum, either alone or in conjunction with the pneumococcus, and it appears probable that, in patients with such an onset, infection occurs through the respiratory passages and ultimately by the blood and lymph streams reaches the intestine, though the condition might perhaps be equally well explained by an early localization of the bacillus in the lung. This type of the fever is not very uncommon, and I have recently observed an interesting outbreak of it in a family, five members of

which, out of six affected, commenced their attack with all the symptoms of lobar pneumonia. The mother and eldest girl had been treated in different wards of the same general hospital for pneumonia for over ten days before they were sent on to the City Hospital, where already two other children were being treated for enteric fever, one of them being an admirable example of pneumo-typhoid. In the meantime two other children died of 'pneumonia' in the Children's Hospital, and there can be little doubt that in these cases also enteric fever must have been present. In this group of cases, then, four different hospital physicians of experience were entirely deceived by the original symptoms of the illness.

As regards *other respiratory complications*, we have already seen that *bronchitis* occurs in a mild form almost frequently enough to be regarded rather as a symptom. *Pleurisy* with effusion, which may be clear, hæmorrhagic or purulent, is occasionally observed. Sometimes, indeed, it is sufficiently well marked to mask the other symptoms of the fever, the chest condition being regarded as sufficient to account for all the symptoms. The pleurisy, moreover, may be the first symptoms of the illness, and I have recently seen a case in which the patient was treated for the effusion and tapped several times over a period of five weeks, at the end of which he was notified as 'observation' for enteric fever, mainly on the strength of a positive serum reaction. There were no obvious symptoms of enteric fever, and the patient looked suggestively tubercular, but the bacillus typhosus was recovered in pure culture from the pleural fluid. Such a case might be described as 'pleuro-typhoid'. *Pneumothorax* has been reported, and, when it occurs, is occasionally associated with venous thrombosis in some other part of the body, which has led to the suggestion that it is due to infarction of the lung with subsequent softening of the infarct and perforation of the pleura. I have not personally seen a case, but both abscess and gangrene of the lung figure in my records. More important, and apparently relatively common in some outbreaks, is *laryngitis*. This is due to ulceration which chiefly affects the posterior wall of the larynx, and starting as a mere erosion of the mucous membrane may ultimately cause extensive necrosis of the cartilages. The condition is especially found in very severe cases of a prolonged type, and often seems to cause very little in the way of obvious symptoms. Indeed, its existence may remain entirely unsuspected during life, and only be discovered on the post-mortem table. The most likely manifestations are hoarseness and pain in swallowing, and sometimes a gradually increasing difficulty in breathing, which in a very exhausted and stuporose patient may almost escape notice. More rarely acute recurrent attacks of dyspnoea, and the coughing up of actual pieces of necrosed

cartilage, may draw attention to the case. Sometimes acute œdema of the glottis appears with great suddenness, and, unless tracheotomy is at once performed, is rapidly fatal. The prospects of recovery are very slight, even when operation gives temporary relief. My own experience of this serious complication is small. Not more than half a dozen of my patients suffered from obvious laryngitis, and in only two did necrosis of the cartilages follow. Both the latter succumbed, one after a tracheotomy. In a few others, slight ulcerations, unsuspected during life, were observed in the post-mortem room. Ulcerations on the soft palate are also described.

Various suppurative and septic complications are apt to occur either during, or after, enteric fever. *Parotitis*, in most cases limited to one side, but occasionally double, is liable to occur in very severe cases, though much less frequently than in typhus. In the few cases which occurred in my series, suppuration followed. The inflammation is probably due to infection with pyogenic micro-organisms from the mouth, and I am inclined to believe that the comparative rarity with which the complication is nowadays observed may be due to the greater attention paid to the cleanliness of the buccal mucous membrane and tongue of fever patients. Twenty years ago, in England at least, cases were relatively more common. Instances of parotitis due to the bacillus typhosus have been reported.

Periostitis is another complication which does not appear to me to be as common as formerly, and, like some other septic conditions, I have seen it occur most frequently in patients whose fever had been unduly prolonged, and who had been somewhat rigidly dieted. Only six instances of it occurred in my present series, the affected bones being the tibia, three cases, and the femur, humerus, and superior maxilla one each. The tibia is by far the most common situation, and several cases came under my notice when I was an assistant at the City Hospital. Periostitis, however, may affect almost any bone in the body, and, in the table given by Keen, it appears that, next to the tibia, the ribs and the femur are most frequently implicated. The typical time for the complication to occur is in convalescence, usually about three weeks after the pyrexia has finally subsided, but it must be recollected that bone lesions, due to the typhoid bacillus, have been described as occurring months or years after the termination of the fever. Sometimes the exciting cause appears to be some trivial injury. Often the condition starts just after the patient has first been allowed out of bed and is attempting to walk. The first symptom is usually pain, and this is apt to keep him awake at night. On examination, the surface of the tibia over a limited area is found to be extremely tender, and a small node or swelling may be appreciated. In most cases the condition goes on to

suppuration, the swelling becoming tense and red. On opening the abscess bare bone will be found exposed, and necrosis with exfoliation of bone often follows. The pus may either contain the typhoid bacillus or septic micro-organisms. It is believed that the bacilli, existing in large quantities in the bone marrow, are enabled to invade the periosteum, if it is in any way damaged by a slight injury or depressed as the result of the thrombosis of a small vein.

The condition known as **typhoid spine** may have some relation to these periosteal inflammations. It was originally regarded as a peri-spondylitis, the periosteum and the ligaments of the vertebræ being supposed to be affected. Suppuration, however, does not occur, as is the case when other bones are inflamed, though, as Wilson suggests, the spinal deformities, which occasionally result, point to the bones being definitely implicated. Radiography has done much to explain the nature of the condition, and the most constant lesion appears to be an alteration of the inter-vertebral discs, which, instead of being represented by clear spaces in the radiograph, show a density equal to, or greater than, that of the vertebral bodies themselves. The peri-vertebral tissue is frequently, but not always, the seat of various alterations in the neighbourhood of the affected discs, the transverse processes with the ligaments and the bodies of the vertebræ being, as it were, implicated in one zone of badly defined ossification. In some instances, indeed, the bodies alone seem to suffer and the discs to remain unaffected, and Rogers, who reports two cases, considers that the condition is in reality an osteo-myelitis due to septic emboli and entirely analogous to the other bone lesions of typhoid fever. It is now, however, generally described as a spondylitis.

Typhoid spondylitis may manifest itself during the illness, but in 65 per cent. of the published cases it appeared in convalescence or shortly thereafter, although in some instances a year or more elapsed before its occurrence. It is a rare complication. Halpenny, for example, noted it once in 1,800 cases; in my own experience of 1,700 cases it only occurred once as a late sequel; and Sir John Moore published recently the only case he has seen in what must be a very much larger number of patients than either of the figures mentioned. From the study of 100 cases collected from the literature Weissenbach and Bonhoure found that it occurred in only one patient under the age of ten years, and from their table it would appear to be exceptionally common between thirty and thirty-five years. It has, however, been observed in a patient as old as sixty years. Women seem to suffer from it much less frequently than men, eight out of every ten of the reported cases being of the male sex.

The symptoms are fairly constant, except for slight variation of details. Pain, sometimes moderate at first, but usually extremely acute, is complained of. This pain is usually lumbar, but it may be of a girdle character, and sometimes radiates to the lower limbs along the line of the sciatic nerve. It may be continuous, but is often spasmodic and apt to be worse at night. Its most outstanding features are its excruciating character and its resistance to all treatment, except that by complete immobilization, e. g. a plaster jacket. Local swelling or redness are unusual. Deviation of the spinal column, either antero-posteriorly or laterally, appears to be the rule. Muscular rigidity is a common feature. There is exquisite tenderness on pressure of the vertebral spines, and spinal pain may be produced by pressure on the shoulders and heels. Cutaneous hyperæsthesia and exaggerated knee-jerks are usually noted. Fever is sometimes well marked and may last for weeks. Mentally the patient is very depressed, and Osler held that in many cases the predominant factor is a neurosis. The prognosis is always good, but recovery is slow, the duration of the condition varying from one month to a year.

Arthritis is a very rare complication ; if it occurs, it is often suppurative and is not infrequently followed by dislocation of the joint. The hip is stated to be the joint most liable. No case has come under my own notice.

Superficial skin *abscesses* and small boils are frequently seen, especially in children. They occur usually in debilitated and exhausted subjects, and are said to be more common in cases treated by the cold-bath method. Abscesses affecting deeper structures have also been described, but are fortunately rare. *Cancrum oris* is occasionally seen in badly nourished children. *Otitis media* is a frequent sequel of the disease, particularly in the young.

A complication of some interest and importance is **cholecystitis**. This was only present in one of my fatal cases, and in that instance the gall-bladder was found to be full of thin pus and contained a few small stones. In two patients the condition was sufficiently acute to require operation, and both made good recoveries. In one of these, the cholecystitis complicated the acute stage of the fever, in the other it supervened in the second week of convalescence. A few other patients in my series showed symptoms suggestive of the condition. Swelling just below the costal margin, tenderness, pain in the right upper quadrant of the abdomen, and sometimes a slight degree of jaundice, point to the presence of this complication. It is well to remember that such a gall-bladder may perforate. In some cases the inflammation is doubtless caused by the irritation of pre-existing gall-stones, and by the action of the typhoid bacillus. We have already seen that the

bacillus itself appears capable of causing the formation of gall-stones, and that a cholecystitis occurring many years after an attack of the fever may depend upon its persistence in the gall-bladder.

Spontaneous *rupture of the spleen* has been reported. The practical interest of this very rare complication is this, that certain typhoid vaccines, such as the autolysate of Vincent, are apt to cause a very marked increase in the size of the spleen, and should be withheld if the organ is unduly enlarged.

An early complication may be *nephritis*. This condition was only present in ten of my 1,700 cases, and in several of these it had existed before the fever commenced. In a recent example the illness started with nephritic symptoms, blood and albumin in the urine being the outstanding feature. The character of the fever, and the diarrhoea which accompanied it, caused typhoid to be suspected, and a positive serum reaction was obtained on the sixth day of illness. On admission to hospital the urine was found to be swarming with typhoid bacilli, and the case terminated on the tenth day, the pyrexia subsiding with the gradual disappearance of blood from the urine. This case appeared to be a true **nephro-typhoid** depending on a localization of the germ in the kidney with only slight systemic infection. Oedema is said to be unusual in these cases, but oliguria, though not present in the patient mentioned, is usually observed. Pyelitis occasionally occurs. It starts with the ordinary symptoms of nephritis, blood and epithelium in the urine, and pus appears later and may be persistent. The typhoid bacillus has been found in the kidney. Cystitis, except to the slight degree associated with typhoid bacilluria, is not seen, so far as my experience goes, except in cases of retention of urine which have been neglected, or have been catheterized. *Orchitis* occurred in three of my cases, and must be regarded as a possible, though uncommon, complication of the disease.

Complications affecting the nervous system are numerous, but for the most part rare. Cerebral thrombosis occasionally occurs. *Convulsions* are not common. Only six patients in my series presented them. They were due to various causes, but all occurred in the course of the fever; none were initial. Meningitis may appear at the onset or during the course of the illness. It may be due either to the typhoid bacillus itself or to pyogenic organisms. In the former case the spinal fluid may be either clear or slightly turbid and contains the bacillus. Two patients in my series suffered from the **meningo-typhoid** of the French authors, the attack commencing with classical symptoms of a meningitis which terminated fatally before the full development of the usual signs of enteric fever. In both the serum reaction was present and the spleen enlarged, and the bacillus was recovered from the meninges. *Meningism* is common in children suffering from severe

attacks, and is probably due to the action of toxins. The fluid remains clear and sterile. *Neuritis* has not been a frequent complication in my cases. When it has been present, it has been nearly always in alcoholic patients and limited to the lower extremities. The most obvious symptoms have been pain, and difficulty in walking. It is an extremely troublesome and persistent sequel of the fever. The condition known as '*tender toes*' is an interesting one. The tips of the toes become hyperæsthetic and cannot even bear the weight of the bedclothes. I have not seen more than a dozen cases, but the complication seems to be common in patients who have been treated systematically with the cold bath. It is, as a rule, short lived, sometimes only lasting a few days. Of more severe nervous sequelæ it will be sufficient to mention paraplegia and hemiplegia.

We have already noted that the mental condition of the patient, after enteric fever, may be weak. Mania and melancholia may both occur, and probably depend upon the anæmic state of the brain. One of my patients suffered from dementia. I had unfortunately no means of hearing the result of her case, but the prognosis of these post-typhoid psychoses seems to be good.

Enteric fever may coexist in the same patient with *other infectious diseases*. Of these influenza and scarlatina are perhaps the most important. It is well, however, to remember that both these conditions may be mistaken for typhoid, and therefore strong evidence is required before a diagnosis of their concurrence with that disease can be made. Erysipelas, as shown in Fig. 41, may also be seen in the typhoid patient, and diphtheria and measles have complicated one or two of my cases. As regards tuberculosis, the two infections occasionally coexist, and phthisis sometimes, but rarely in my own experience, occurs as a sequela.

Enteric fever and pregnancy. It may be roughly estimated that from half to two-thirds of pregnant women suffering from enteric either abort or are prematurely delivered. It is usually stated that, the later on in pregnancy the fever appears, the more certain is interruption of pregnancy to take place, but no stage is immune from this accident. Abortion has been explained as due to endometritis, to prolonged high temperature, and to the infection of the foetus with the typhoid bacillus. The foetus is not often expelled before the end of the second week, but usually later; occasionally, indeed, in convalescence. In cases of merely premature delivery the child is in most cases born dead, or, if alive, seldom lives many hours. The prognosis for the mother is as a rule not particularly serious, the mortality of 324 cases collected by Sacquin only amounting to 11 per cent.; in other words, barely more than might be expected in the

fever. In the only maternal death which I have witnessed, flooding and subsequent profound exhaustion precipitated the end.

The typhoid bacillus has been isolated from the blood of the foetus in several instances, but it is by no means always to be found, and it has been suggested that some damage to the placenta, such as might be caused by hæmorrhagic infarcts, is necessary before the micro-organism can pass through it. Agglutinins can, however, filter through the placenta, and the blood of an uninfected foetus may therefore give a positive serum reaction. It seems reasonable to suppose that the toxins in the blood are the real cause of the death of the foetus. In the cases which I have examined after death there were no lesions of the bowel.

DIAGNOSIS. The insidious invasion of enteric fever, its liability to resemble various other acute diseases, and the extraordinary varieties of type which may be exhibited by its course, combine to render diagnosis a matter of considerable difficulty. It may be said with justice that the only absolute proof of its presence in a given case is the isolation in pure culture of the bacillus, typhosus from the blood of the patient under consideration. Short of this, our diagnosis must depend on the appearance, in varying combinations, of certain signs and symptoms, none of which are constant, and of which many are, not infrequently, absent. We have also, in the serum reaction, a test which, if not infallible, is in the vast majority of cases of the greatest assistance.

Clinical diagnosis. Putting aside in the meantime the different bacteriological methods which have so often to be employed to finally decide the nature of a case, it will be well in the first place to consider the means at our disposal for coming to a definite conclusion without their aid. The commencement of the fever is so insidious that, as a rule, the case is seldom seen in the first few days of the fever. The average enteric patient can keep his feet, and often do his work, for the first week or ten days of his illness. The lower he is in the social scale, the later he is likely to call in medical aid ; but, when he has ultimately come under observation a great deal may be learned from his *history* of the symptoms from which he has suffered. These fall naturally into two groups ; firstly, general symptoms pointing merely to fever and toxæmia, and secondly, various local symptoms pointing to derangement of the alimentary or other systems. Thus every patient who suffers from fever, whatever be its cause, is liable to complain of loss of appetite, loss of sleep, feelings of chilliness, headache, and indefinite pains in the trunk and limbs ; and such symptoms are naturally complained of at the commencement of typhoid, as they are in the other febrile conditions. But in addition to these general symptoms

the enteric patient probably complains of either diarrhœa or constipation ; the bowels, indeed, are very seldom normal. Many suffer from abdominal pain or uneasiness. Epistaxis is a frequent symptom of the invasion period, occurring, in my experience, in nearly 30 per cent. of the cases. Much more rarely, cough, due to the bronchial catarrh which is almost invariably present, may have been troublesome enough for the patient to give it a prominent place in his recital of the history of his case.

Now on studying these two groups of symptoms, the general and the local, we may deduce from the first that the patient under consideration has probably been suffering from a febrile condition ; and, if the temperature at the moment of examination is found to be elevated, it is natural to conclude that we are dealing with a case of continued fever, dating from his first symptom. And, in addition to this, if even one of the symptoms mentioned above, either abdominal pain, diarrhœa, or epistaxis, is noted in the patient's history, there is a fair chance that he is suffering from enteric fever. Constipation, though perhaps even more frequently present, does not give such a valuable suggestion, as it is liable to complicate many febrile disorders. Cough, again, is misleading, and would turn our thoughts towards some pulmonary affection.

The student who has been accustomed to see cases of enteric fever lying in bed in a hospital ward is apt to forget that in private practice the patient is often first seen in the doctor's consulting room. Indeed, he may be able to return there on several occasions before he gives in and takes to bed. Such a patient frequently attributes his discomfort to some digestive trouble, and the tendency is often, in view of the appearance of the tongue, to treat him for simple gastric catarrh. The late Sir Thomas Grainger Stewart used to warn his students that, if such a case did not at once improve under bismuth, rhubarb, and soda, enteric fever should be suspected and the patient's temperature taken. This simple precaution is often omitted, as the comparatively slow pulse of the enteric patient makes the physician apt to assume that there is no pyrexia present. Another misleading complaint may be cough, and it is not at all uncommon for medical advice to be sought for this reason alone. If, however, the medical attendant is fortunate enough to see the case first in bed, there should be much less chance of the real nature of the malady being missed. The appearance and facial expression are often very suggestive. The slight hectic flush, wide pupils, and apathetic look, usually to be seen in the first fortnight of the fever, will, when the patient is seen in the more suggestive surroundings of the sick-room, often awake the suspicions of the practitioner.

If any record of the temperature has been kept, which is unfortunately

not usual, a chart showing the gradual zigzag rise, so frequently noted in the fever, would naturally go far to make a positive diagnosis. But some cases of enteric commence singularly abruptly with high pyrexia ; and while we may still say with Wunderlich that a patient presenting a temperature of 104° on the first day of his illness is probably not suffering from enteric, we must be prepared to meet occasionally with exceptions to this rule. In any case, we should expect at the end of the first week to find a fairly high temperature, often 103° or 104° at night, and showing a good morning remission. The pulse relation is of great importance in diagnosis, particularly in adult males. Relative slowness is not so frequently seen in females, especially in the young. Children have nearly always a pulse proportionate to the pyrexia. Dicrotism is a valuable indication in both sexes and is much more often met with in enteric than in the other acute fevers. But, even in male adults, too much stress must not be laid on its absence in a severe case in the third week, by which time also the pulse rate has often regained its normal ratio to the temperature level. During the first fortnight of enteric fever it is unusual to find the respirations very frequent, and, if they exceed twenty-eight or thirty in an adult, there is a presumption that the symptoms depend upon some pulmonary lesion. Later in the course of the fever, if the case is a severe one, the respiration may, of course, be rapid as the result of hypostatic congestion, but usually a medical man has been called in before this supervenes.

While we usually associate a furred tongue, dry in the centre and with clean red tip and edges, with the early stages of the fever, it is well to remember that similar appearances are often present in other febrile conditions. The examination of the abdomen will always furnish us with the most valuable information. Tumidity is so much the rule that a case presenting a hollow or flat abdomen is usually not enteric. Tenderness in the right iliac fossa, when the symptoms point to enteric fever, is a useful corroborative sign. It is, however, by no means always present. The value of gurgling has been much overrated. In examining the abdomen the main point is undoubtedly the recognition of spots. They are probably present in most cases in the early days of the second week. Their absence is of no value in assisting the diagnosis. Their presence, if they are typical, is practically final. Occasionally spots are noticed which may not conform in appearance to the classical descriptions. In the records of my own cases I find 'doubtful' or 'suspicious' spots not infrequently noted, and it is interesting that the vast majority of the cases in which they were observed were ultimately found to be enteric. It would therefore seem that the presence of even atypical spots is of considerable value in diagnosis.

Enlargement of the spleen is practically invariable, and the organ can often be palpated with ease. Should no increase in size be made out, the suggestion is that the case is not enteric. The occurrence of the classical ochre stools is in favour of a positive diagnosis, but it must be remembered that similar appearances may be presented by the stools of other acute fevers, particularly if milk is badly digested. The absence of the abdominal reflex is a very suggestive sign if nervous and abdominal conditions can be excluded. But its presence is quite compatible with even the acute stage of the illness, and several of my patients, chiefly females, presented it throughout their whole course.

Sufficient stress is, perhaps, not laid on the presence of slight bronchitis and bronchial catarrh. A case of continued pyrexia, in which no obvious symptoms of enteric are observed, but which presents a slight degree of bronchitis, often turns out to be enteric. Again, any patient who, in addition to continued high temperature, suffers from hæmorrhage either from the nose or from the bowel is, in the first instance very probably a case of enteric fever, and, in the second, if hæmorrhoids are excluded, almost certainly so. Lastly, complaints of giddiness in the first week of the fever, and obvious deafness in the second, are, at least, suggestive signs.

The effect of the toxins on the inhibitory action of the vagus with the relative slowness of the enteric pulse has been made use of by Marris as a means of diagnosis, particularly in inoculated subjects. He has devised the *atropine test*, which consists in first taking counts of the pulse for ten consecutive minutes, then injecting hypodermically $\frac{1}{33}$ of a grain of atropine, and twenty-five minutes later counting the pulse for ten minutes more. If the mean of the counts after injection exceeds that of the original counts by more than fourteen, the test is negative; if the increase, or 'escape' is less than that figure, it is positive. My own very limited experience of this test is, on the whole, confirmatory. Two Japanese workers, Matsuo and Murakami, have reported results contrary to those of Marris.

Only a certain number of the symptoms above detailed may be found in any given case. It is the fact that so many of them are often in default which gives to the diagnosis of enteric fever both its uncertainty and also its chief charm. In the vast majority of cases a conclusion can be reached by observation of these points alone. A diagnosis may also often be arrived at by the exclusion of any other possible cause of the fever. To assist us further, however, short of the actual isolation of the bacillus, we have the diazo reaction of Ehrlich, the information to be obtained from a blood count, and the serum reaction or Widal test, all of which will be referred to later (p. 317).

Differential diagnosis. The difficulties of diagnosis are well illustrated by the table below showing 607 cases, admitted to the Edinburgh City Hospital, either intimated as enteric fever, or sent in as 'observation' for that disease, but ultimately recognized as suffering from other conditions. As is only to be expected, certain diseases occur on this list much more frequently than others, and acute lobar pneumonia occupies first place, 123, or about a fifth of the whole number of wrongly diagnosed cases, being instances of this infection. Of other conditions affecting the respiratory system broncho-pneumonia accounted for forty-eight cases, and no less than twelve patients suffered from nothing more than pleurisy with effusion. The large numbers of patients classed as 'constipation' appeared to be suffering from sapræmia. The cases described as 'diarrhœa' were chiefly various forms of enteritis in young children, the illness being usually due to improper feeding, or food poisoning.

If the table is analysed it will be found that no less than seventy-eight instances of tubercular infection occur on the list, tubercular meningitis being the most common. Conditions affecting the respiratory system are very frequent, 218 patients, or more than one-third of the whole, representing this class. Abdominal and pelvic conditions, exclusive of diarrhœa and constipation, account for thirty-eight cases. Cerebral inflammations are noted in thirty-nine patients. It is natural that certain acute infections should often be mistaken for enteric. Of these influenza provides 112 cases, and typhus, which, but for its rarity, would doubtless have headed the list, twenty. The cases of acute rheumatism were, in most instances, at the time of their admission in the 'typhoid state'.

TABLE A

SHOWING THE ULTIMATE DIAGNOSIS OF 607 CONSECUTIVE CASES ADMITTED TO CITY HOSPITAL
WRONGLY INTIMATED AS ENTERIC FEVER OR AS 'OBSERVATION' FOR THAT DISEASE

Acute Lobar Pneumonia	123	Appendicitis	8
Influenza	112	Acute Rheumatism	7
Broncho-pneumonia	48	Cerebro-spinal Meningitis	6
Constipation and Sapræmia	48	Other forms of Meningitis	8
Diarrhœa	40	Local Tubercular Lesions	6
Tubercular Meningitis	25	Malignant Abdominal Disease	4
Acute Miliary Tuberculosis	22	Abscess of Liver	2
Typhus	20	Cholecystitis	1
Phthisis	13	Ulcerative Colitis	1
Tubercular Peritonitis	12	Bacillus Coli Infection	3
Pleurisy with Effusion	12	Malta Fever	2
Inflammations of Female Pelvic Organs	10	Kala Azar	1
Septicæmia	9	Other conditions	64

The great deduction to be made from these figures is that, however much a case looks like enteric fever, it is always a wise precaution to examine the chest and to exclude acute pulmonary conditions before coming to a diagnosis. In many of the patients on the list the rate of the respiration alone should have attracted attention. Secondly, it is well to recollect the frequency with which tubercular conditions simulate the disease; and, lastly, the possibility of the abdominal tumidity of a feverish patient being due to some local cause should never be forgotten. A study of the table will suggest other sources of error. Except for the fact that it does not include any example of ulcerative endocarditis, it may be taken as fairly representing the conditions liable to be mistaken for enteric fever in this country.

Lobar Pneumonia is, as we have seen, very often confused with enteric. This depends chiefly upon the comparative frequency with which the 'typhoid state' supervenes in this condition, and also on the fact that the appearance of definite physical signs is, not uncommonly, considerably delayed. A large proportion of the cases intimated as enteric fever are found to have their lesions at the apices, and it is in this particular variety of pneumonia that head symptoms are often most pronounced, and physical signs most indefinite. It must be remembered, moreover, that enteric fever itself sometimes starts with sharp pulmonary symptoms, and that pulmonary complications are not at all uncommon. A pneumonia, then, may be recognized as such, and yet the case be regarded as one of enteric fever.

As a general rule the onset of lobar pneumonia is much more sudden and more definitely marked than that of enteric. In most cases the acceleration of the respiration should arouse suspicion, and, in male adults particularly, it is usual to find the pulse more rapid than it is likely to be in the early stages of enteric. Dicrotism, again, is not a frequent symptom. The presence of herpes on the lips is a strong point in favour of pneumonia. In typhoid it is, in my experience, extremely rare. Typical rusty sputum is of great help in diagnosis. Theoretically a high leucocyte count would strongly suggest pneumonia, but it would also be present in an enteric with a pulmonary complication. The diazo reaction is not infrequently present in pneumonia. It is, however, rarely absent from enteric at the period the two illnesses are likely to be confused, and its absence therefore would negative a typhoid diagnosis. If the case is in reality one of enteric, it is often at a stage at which we cannot confidently count on a positive serum reaction, so this test, usually so reliable, cannot be absolutely depended on. The practitioner should remember that the indiscreet administration

of milk in large quantities to patients suffering from the high pyrexia and weak digestion of such a disease as pneumonia will often cause marked abdominal tumidity and discomfort, and is not unlikely to produce a fair imitation of the typical 'pea-soup' stools. I am inclined to believe that the absence of the abdominal reflex may be regarded as presumptive evidence in favour of enteric, where the diagnosis lies between that disease and pulmonary conditions.

Broncho-pneumonia is a not infrequent source of wrong diagnosis in children. The temperature occasionally imitates the enteric curve very closely, and general symptoms of toxæmia and wasting may heighten the resemblance. But the rapidity of the breathing, often extreme, the expansion of the *alæ nasi*, the slight grunting sound on expiration, and the tendency to cyanosis should in most cases clear up the difficulty, even if the physical signs are most indefinite. The spleen, moreover, seldom shows the marked enlargement so characteristic of typhoid. Looseness of the bowels and abdominal tumidity are, however, extremely common, and the absence of spots in children of under ten years of age is of course of no value in diagnosis.

We have seen that the tubercular conditions are very liable to be mistaken for enteric fever. The most difficult to distinguish is unquestionably *Acute Miliary Tuberculosis*. Of the twenty-two cases noted in the table very few were recognized till they had been a week or more under observation in hospital. Some were accepted as instances of enteric until several negative results were given by the Widal test. In these the relation of pulse to temperature was similar to that of enteric fever, and the course of the pyrexia itself showed the type usually associated with the period of advance of the latter disease, that is to say, regular and well-marked morning remission. The diazo reaction is valueless here. Practically all cases of acute tuberculosis give it. The respiration in many patients is unaffected till towards the end, when its frequency is usually suddenly and markedly increased. Physical signs on auscultation may be altogether wanting. The most useful indication is a certain duskiness or lividity of the face and extremities, which is often noticed, and in several of my cases first attracted attention to the true nature of their condition. The spleen is not so constantly enlarged in tuberculosis as in enteric fever, and, if there is no apparent enlargement, suspicions should be aroused. Unless the cerebral membranes are affected the abdomen is not retracted. It may even be meteoric. The presence of typical spots would, of course, decide the question on the one hand, as would the recognition of tubercles in the choroid on the other, but an additional difficulty lies in the fact that the two diseases

are said to occasionally coexist. My own experience leads me to the belief that Widal's reaction is often the only method of diagnosis possible. Should this remain persistently negative, and the diazo reaction continue to be brilliantly positive, a diagnosis may be justified. The isolation of the typhoid bacillus from the blood would form definite evidence of enteric fever, and a persistently low leucocyte count with a relative increase in mononuclears would favour a diagnosis of that disease.

The difficulty of distinguishing *Tubercular Meningitis* from enteric fever is often a very real one. We have seen that in children particularly there is hardly a symptom of meningitis which may not be present in typhoid. In doubtful cases lumbar puncture should always be practised, but, as the fluid is clear in both conditions, all that can be hoped is that the tubercle bacillus may be found on microscopic examination, and this can by no means be regularly expected even in a recognized tubercular case. Vomiting is likely to be a prominent symptom in the history of a meningitis case, and convulsions, though sometimes seen in enteric, are much more common in the cerebral condition. The old axiom, that headache ceases when the delirium of enteric fever begins, is of some value, especially in older children. Persistent 'crying with the head' is certainly more common in meningitis, when delirium is once established. A very slow pulse, hardly raised above the normal rate, or even below it, would certainly suggest meningitis, but in many cases of that condition the pulse is at least as rapid as that of enteric usually is in children. Kernig's sign, if well developed, is a great argument in favour of the diagnosis of meningitis, but I have certainly seen it, though perhaps not very well marked, in enteric fever with severe head symptoms. Retraction of the head is also in favour of a true meningeal inflammation, but it nevertheless is occasionally seen in typhoid, and general rigidity of the muscles is not at all infrequently observed in that disease. Retraction of the abdomen, on the other hand, is not in the least likely to occur in the course of enteric fever, while it is relatively common in tubercular meningitis, in which, however, a tumid abdomen is by no means impossible. The recognition of spots will sometimes settle the question, but the age at which we are accustomed to see meningeal symptoms develop in typhoid is one at which the typhoid eruption is frequently absent. Optic neuritis or the presence of tubercles on the choroid are definite evidence of a meningeal inflammation. The leucocyte count in tubercular meningitis is said to be high. It is interesting to know that the two diseases may run concurrently. I remember a case which showed post mortem the lesions of both infections. During life the only point which suggested enteric was a strong and persistent positive Widal reaction.

More rarely, in my experience, is *Tubercular Peritonitis* liable to cause confusion, but, as will be seen in the table, twelve cases have come under my observation. The disease is only in its early stages likely to resemble enteric fever. At this time the appearance and expression of the patient may be very suggestive, and the temperature chart may be quite compatible with a diagnosis of mild enteric. When, however, fluid is appreciable in the abdomen, or glands become palpable, the difficulty is completely overcome.

As regards *other tubercular conditions* there is not much to be said. The cases of phthisis which have been admitted to the City Hospital as enteric fever were for the most part in the early stages of their illness, and suffered from an unusual amount of pyrexia. In facial appearance there was not much to distinguish them from enteric, but there was little difficulty in recognizing the condition. A few cases were admitted in the 'typhoid state', and their medical attendants were, doubtless, aware that cavities existed, but wrongly suspected that enteric fever was also present. The fever caused by early tubercular disease of a joint, usually the hip, has also caused several instances of wrong diagnosis, and this emphasizes the necessity of a thorough examination before notification. It is probable that several of the twelve cases of *pleurisy with effusion*, noted in the table, were also tubercular. That this mistake should occur so comparatively frequently has always puzzled me, as, except for continued pyrexia, there was little about any of them to suggest enteric fever, and the physical signs were fairly obvious in all the cases. The frequency with which cough is set up, when the patient is turned in bed, should of itself attract attention. It is hard to see how the condition could have been missed, had the chest been examined, as it should be, as a routine.

Acute abdominal and pelvic conditions may be mistaken for enteric fever, but in most cases the localization of the tenderness, and the recognition of resistance, or of actual tumours, on palpation will put the practitioner on his guard. *Appendicitis* may be diagnosed as enteric fever, or the reverse may take place, and I have had under my care four cases of typhoid on which operations for appendicitis were performed before admission. Although undoubtedly there may be general tenderness in the appendicitic area in enteric, it is seldom so acute, or so localized at McBurney's point, as is the case in appendicitis. The history of the patient should also be of great assistance in these cases, and the absence of an enlarged spleen, of spots, of dirotism, and of enteric symptoms generally should assist the diagnosis. The same applies to such a condition as *cholecystitis*, though here the difficulty may be greater, as the condition may occur as a complication

of enteric fever, and is not infrequently seen as a remote sequel to it. As, in such cases, Widal's reaction may be positive if the bacilli become in any way active, the difficulty of diagnosis may be very great. Still it is to be expected that some history of a previous attack will be obtained, and, second attacks being rare, this should prejudice us in favour of a mere local inflammation. The general circumstances and history of the case should, as a rule, prevent mistakes regarding *pelvic cellulitis*, endometritis, and other gynecological conditions, but it is well to recollect that errors have been made. Enteric fever is sometimes very closely simulated by *ulcerative colitis*, in which disease the appearance of the patient, the continued fever, and the bowel symptoms are often misleading. But the temperature is much more irregular than that of typhoid, and the stools contain streaks of blood and shreds of mucous membrane much more frequently. There are, again, more signs of irritation of the lower bowel and more liability to tenesmus, and ulceration of the rectum may be not infrequently felt on digital examination. The *summer diarrhœa* of children is occasionally notified as enteric, and at times the distinction is difficult. The disease, however, runs a shorter course and its onset is usually sudden. It is not probable that the spleen will be much enlarged. The bowel symptoms are, on the whole, much more severe, and the suggestion of general toxæmia less. Indeed, in many local inflammatory conditions affecting the abdominal viscera this discrepancy between the severity of the local and general symptoms should be of great assistance in diagnosis. It may be well to remark here, that the absence of the abdominal reflex, usually a sign suggestive of enteric, must not be relied upon to distinguish that fever from local abdominal inflammations, as in these conditions the reflex is usually abolished.

A case of *ulcerative endocarditis* does not figure in my table of mistaken diagnosis, but there appears to be no doubt that it may resemble enteric fever very closely. The character of the pulse, however, will usually attract attention to the heart, and, endocarditis being rare in enteric, the presence of murmurs, varying much from day to day, will suggest the real nature of the case. Should old-standing cardiac disease be present, the difficulty of diagnosis might be very great. Embolic lesions in other organs would, of course, point to endocarditis. It may be remarked that the spleen is said to be frequently enlarged in this condition.

What has been already said regarding tubercular meningitis applies for the most part to other *meningeal inflammations*. Lumbar puncture, which should always be practised, if there is reasonable doubt, will give positive evidence of meningitis due to infection with the meningococcus, the pneumococcus, or various septic micro-organisms. In all these cases the fluid will

be turbid, and microscopic examination of a film is an easy matter. The extremely sudden onset of cerebro-spinal meningitis, the frequency with which herpes, so rare in enteric, occurs in that disease, and the early development of marked head symptoms should, in most cases, make the distinction. As regards the septic varieties of meningitis, a careful examination of the ears may put the medical attendant on the right track. It must be noted that the abdominal reflex is often absent in meningitis.

So far as the acute infectious diseases are concerned, the differentiation of enteric fever from *typhus* will cause most difficulty. The distinction between the two fevers is fully discussed in the section on typhus.¹

When intestinal symptoms accompany an attack of *influenza*, some difficulty may arise. The fever, however, is more sudden in its onset and much shorter in its course than enteric, seldom lasting more than ten days. Persistent frontal headache, often felt behind the eyes, and marked pain in the back are more suggestive of it than of enteric, and the presence of coryza at the outset would be a strong point in its favour. The spleen, moreover, is not often much enlarged. On the other hand, epistaxis may occur in influenza, and the pulse is often relatively slow, though it is seldom dicrotic.

Scarlatina of the prolonged² typhoid type is sometimes singularly like enteric fever. If, however, it is thoroughly understood that this type of scarlatina exists, there should not, as a rule, be much difficulty in making the distinction. The definite history of the exanthem, which can usually be obtained, the presence of desquamation, corresponding in its situation with what might be expected from the duration of the case, and the absence of spots and of a positive serum reaction, should be sufficient to exclude enteric fever. More rarely the presence of an erythematous rash in the first week or two of a case of enteric may cause confusion, but in such a case there are no corresponding signs to be found in the tongue or fauces. It should be recollected that the two diseases may coexist. I remember once seeing typical rose spots appearing through the fading rash of an undoubted case of scarlatina.

In countries where *malaria* exists, cases may arise which will cause considerable difficulty. Osler stated that it is particularly the autumnal form of malaria which is liable to be confused with enteric fever, as in this variety definite chills may be absent, and the remissions of temperature may be trivial. Parasites, moreover, may not always be found in the blood. In some cases of *secondary syphilis* there is sufficient fever to give a suggestion of a mild case of enteric. If the existence of the disease is not suspected, this more of fever is all the more readily mistaken, and a diagnosis of typhoid

¹ See p. 246.

² See p. 110.

may be made by a process of exclusion and by the possible presence of a roseolar eruption. The latter, however, is not likely to resemble closely the rose spots of enteric fever. No case of this kind has come under my own notice, but Rolleston has described some interesting examples. It is a possibility of error which it is well to keep in mind.

Pyæmia and septicæmia are also sometimes mistaken. As a rule, however, the cause of the fever can be obtained by careful inquiry, or the site of infection discovered by examination. Repeated rigors, profuse sweats, and great variations of temperature should arouse a suspicion of some pyæmic process, and often a purulent focus will be found. Some cases of puerperal septicæmia are not unlike enteric fever, but, although the latter sometimes complicates the puerperium, a fever commencing shortly after child-birth is more probably due to septic causes. Should the lochia be fetid, and the uterus tender, little difficulty will arise, but in many cases of puerperal infection these signs are absent. The onset, however, is more sudden than that of enteric, and high levels of pyrexia are reached earlier in the disease. The pulse is also rapid from the first. Splenic enlargement is usually only slight. It is interesting to note that since puerperal septicæmia has been made a notifiable disease we have admitted to the City Hospital three cases of enteric fever wrongly intimated as 'puerperal'.

It will be sufficient to name *other conditions* which have been confused with enteric fever. They are, acute delirious mania, Malta fever, relapsing fever, kala azar, Weil's disease (epidemic jaundice), trichiniasis, tonsillitis, diphtheria, osteomyelitis, and acute rheumatism.

Subsidiary methods of diagnosis. There is no doubt that the *dialo reaction* of Ehrlich is a most useful addition to the means at our disposal for diagnosis. Being a very easy test to carry out, it is curious that it is not more used in general practice, as it is particularly in the early days of the fever, before a patient is likely to be removed to hospital, that the reaction is most persistently present. To perform the test two solutions are required, first a saturated solution of sulphanilic acid in dilute (1-20) hydrochloric acid, secondly a one-half per cent. solution of sodium nitrite. I find that the reaction works best, and most consistently, if performed as follows: Fill a third of an ordinary test tube with urine, and add an equal bulk of the sulphanilic solution. Then add one, or at most two, drops of the nitrite, and shake up the mixture till a good froth is obtained. Now render alkaline by allowing a solution of strong ammonia to trickle gradually into the tube. The froth in a negative urine remains pale or may be coloured bright yellow. In a urine which gives the reaction, however, it becomes a beautiful rose pink, the body of the urine becoming deep crimson in colour. In a negative

reaction the urine is merely dark orange, and shows no pink or crimson tints. It is often easier to judge the result of the test by watching the froth alone, as a highly pigmented specimen sometimes causes difficulty if the colour of the urine itself is alone regarded. It is very necessary that the solutions used should be comparatively fresh. The nitrite solution, in particular, deteriorates rapidly and cannot be trusted after about a fortnight. The other important point to remember is that the best results are obtained if only very little of the nitrite is used.

A positive reaction may be found in the urine of an enteric case as early as the fourth day, and it is unusual for its appearance to be delayed beyond the sixth. During the second week it is almost always present, and it is only after the fourteenth day that it is liable to be found wanting. In many cases, however, it persists throughout the period of advance, and is sometimes obtainable even in the period of defervescence.

It must, of course, be remembered that the reaction is found positive in many other conditions. It is almost invariably present during the eruptive period of measles, but that does not affect its value as a useful test in typhoid diagnosis. Unfortunately, however, it is practically always present in typhus, and it is usually to be found in cases of miliary tuberculosis. It is just these two diseases which it is particularly difficult to distinguish from enteric fever, so the test has a very serious limitation in that respect. A positive reaction may be frequently obtained in scarlatina, being most liable to appear in more than averagely severe cases. More rarely is it present in lobar pneumonia. As regards tubercular meningitis and phthisis, it may be given by the urine of both diseases, especially when the case is approaching a fatal termination. It is supposed to depend upon some abnormal decomposition of protein.

The chief value of the test, in my view, is rather its absence than its presence. A case of continued fever, which at any time between the eighth and twelfth days fails to give the reaction, is in all probability not enteric fever. On the other hand, when the reaction is positive, it is necessary to exclude the eruptive fevers, miliary tuberculosis, and pneumonia, before assuming that the case is one of enteric. If these diseases are eliminated, a case giving the reaction is more likely to be one of enteric fever than anything else,—than influenza, for instance. The presence of the reaction in the later stages of the fever may be of some corroborative value, when other signs point to a typhoid diagnosis.

A reappearance of a positive reaction may be expected when relapse occurs in the convalescence of enteric fever. It is rarely absent from the third day onwards. It is useful in this connexion as indicating that a true

repetition of the fever is to be expected, as it does not occur during recrudescence of pyrexia due to constipation, overfeeding, and other similar causes.

The Moriz-Weiss reaction, in which a solution of permanganate of potash gives a bright yellow colour to the urine, and that of Russo, in which 4 drops of a 1-1,000 methylene blue solution turn 5 c.c. of urine emerald green, do not in my experience compare in usefulness with the diazo reaction.

While, as we have seen, leucopenia is the rule in an uncomplicated case of enteric fever, it is most frequently the complicated cases which give trouble in diagnosis, and I must admit that *blood counts* are often disappointing. Leucopenia is not by any means always present in the first week of the fever, when aid is needed most, and a case complicated with pneumonia will often give a high count. On the other hand, I remember a pneumonia in the typhoid state which had a count of 5,000 only. These anomalies make it difficult to say more than that a low count with a relative increase of mononuclears is good corroborative evidence in a doubtful case.

Bacteriological diagnosis. The isolation of the bacillus typhosus is the only certain evidence of enteric fever, but, from the point of view of the general practitioner, this method of diagnosis can only be regarded as what Widal has termed 'un procédé de luxe'. It should be performed by a skilled bacteriologist, if much weight is to be attached to the result. The bacillus can be isolated from the blood, the rose spots, the urine, or the stools. As regards the *blood*, positive results are now obtained in a very high percentage of cases. The points to be observed are, firstly, to take a comparatively large quantity of blood, as the bacilli are present only in small numbers; and, secondly, to dilute it thoroughly in a liquid medium, as the growth of the bacilli will be hindered by the presence of too much blood in the medium. The needle of a sterilized syringe is inserted directly into a vein at the bend of the elbow in the direction of the venous circulation, and 10 c.c. of blood is gently withdrawn. This should be added, preferably at the bedside, to 200 c.c. of alkaline bouillon or, as Gay recommends, to the same quantity of 10 per cent. bile bouillon, the addition of bile being particularly favourable to the growth of the bacillus. If the medium becomes turbid it can be plated out, or smears may be made on agar in twelve or even six hours. Gay has obtained 73 per cent. of positive cultures in the first week and 80 per cent. in the second, the figures falling to 53 in the third, 40 in the fourth, and 33 after the fourth week. Blood cultures seem, then, to be most generally successful if practised in the first fortnight of the illness, and this adds much to their practical value as a method of diagnosis.

To isolate the bacillus from the *stools* it is also desirable that the cultures be made early in the fever. After necrotic changes have commenced, positive

results are less easy to obtain. Recent researches have rendered this particular method more reliable, and the use of the method recommended by Conradi and Drigalski is chiefly responsible for this result.

It is questionable if much is to be gained by cultivations made from the rose *spots*. If the eruption is at all characteristic, the information obtained is superfluous, unless indeed the case is one due to paratyphoid infection. We have seen that bacilli occur frequently enough in the *urine* to make cultivations from that secretion useful in a doubtful case, particularly if the patient has been several weeks ill. Occasionally, however, positive results can be obtained quite early in the fever, and Gwyn in three cases secured cultures before a positive serum reaction was present.

The serum-reaction test. While the cultivation of the bacillus typhosus from the blood or the stools may be the most accurate method of diagnosis, far the most convenient is undoubtedly that of the serum reaction, usually associated with the name of Widal. It is very easy to perform this test, and, although it is not to be relied upon in the early days of the fever, it is wonderfully accurate in finally settling the nature of the case in doubt. Unfortunately, simple though it is, it requires a freshly incubated culture of the bacillus, and therefore is unsuitable for the general practitioner to carry out for himself. There are so many laboratories, however, which are ready to do this class of work that this can hardly be regarded as a bar to its general use, and in a hospital which possesses an incubator any house physician should be able to employ it.

The microscopic method which I was for many years accustomed to use is as follows: The stock cultures of the bacillus typhosus are kept on agar at ordinary room temperature. From twelve to eighteen hours before the test is required a subculture is made on agar and incubated at 37° C. Within the time named the culture has grown sufficiently for a loopful to be scraped from it. This is stirred into a small quantity of sterilized beef bouillon in a watch-glass, and it is with the emulsion of bacilli, so procured, that the test is performed. Great care must be taken to see that no lumps of culture are visible in the emulsion, which should show a uniform turbidity. I find cultures grown on agar, and transferred in this manner to bouillon, act more satisfactorily than a bouillon culture, and have the further advantage that the agar tube remains as a stock culture from which subcultivations may be made at some later date.

The thumb of the patient is carefully cleansed, and is pricked just above the nail. The blood is drawn up into an ordinary leucocytometer pipette to the mark just below the bulb. The point of the pipette is then wiped, and sterilized beef bouillon is sucked up till the bulb is filled, after which the

instrument is shaken. The pipette now contains one part of blood to ten of bouillon. The mixture is then ejected into a U-shaped tube, previously bent for the purpose in a Bunsen flame, and the tube is placed in a centrifuge. This brings the corpuscles down to the bend of the tube, leaving the clear diluted serum above. The process of centrifugalization need not be very complete, as a few blood corpuscles greatly assist in the focusing of the microscope afterwards.

Assuming that it is intended to subject the bacilli to the action of serum diluted to 1 in 30, one drop of the 1 to 10 diluted serum is placed in a celled slide and mixed rapidly with two drops of the emulsion of bacilli from the watch glass. It will be noted that the mixture contains an indefinite number of typhoid bacilli, moving in a medium consisting of one part of blood serum to thirty of beef bouillon. To obtain higher dilutions a greater number of drops of the emulsion must be placed beside the drop of diluted serum on the slide, or the blood may, at the time of taking, be diluted to 1-20 in the pipette. If preferred, the drops may be mixed on a cover-slip, and the examination made with a hanging drop. The preparation is then examined under an ordinary high power. An oil immersion lens is unnecessary, and, indeed, unsuitable.

If the blood be that of an enteric patient, the bacilli, at first actively motile, are seen gradually to lose their motility. They cease to move rapidly across the field, sometimes commence to spin violently, and begin to show a tendency to adhere to each other. First, merely stuck together in twos and threes, these small groups become joined to each other, until after a period, varying from a few minutes to several hours, the microscopic field presents several large colourless masses, consisting of agglutinated bacilli, with spaces perfectly free from moving bacilli between these clumps. In a certain proportion of cases the clumps may be joined together by long strings of motionless bacilli, giving a reticulate appearance to the reaction. If the serum is negative, the micro-organisms retain their motility and move actively through the field, showing no tendency to agglutinate.

A more suitable method of collecting the blood in general practice is to take it in a capillary glass tube, provided, if possible, with a small bulb. This may be hermetically sealed and sent, by post if necessary, to a laboratory. The serum separates from the clot in the bulb, and may be diluted to the required extent by the use of graduated capillary pipettes, or, more roughly, by taking a loopful and adding as many loopfuls of a bouillon emulsion as may be required. Vaccine tubes are often used to collect blood, and, if they are of fairly large calibre, are not unsuitable.

If accurate results are to be expected, it is well to bear in mind several

important points in performing this test. *Stock cultures* must not be subcultivated too frequently ; otherwise the culture tends to become attenuated, and may show false clumping or a partial reaction with a serum which is quite negative if a reliable culture is employed. I make my subcultures from stock tubes which were inoculated not less than two months previously. The *subculture* with which the test is performed should never be more than eighteen hours old. The younger it is the greater is the motility of the bacilli and the cleaner the reaction. Young cultures are usually rich in very long and highly motile forms. The *dilution* should never be less than 1 in 30, a strength which has always in my hands given consistent results, but which is even lower than that usually recommended, most writers preferring 1 in 50 as a minimum. I have never noticed much change in the microscopic appearances after the first hour. If the germs are motile then, they usually remain so as long as they have fluid to move in. But many authorities lay great stress on a *time limit*, considering that delayed reactions are unreliable. It is well therefore to pay no attention to reactions which fail to appear within the hour. As a matter of fact half an hour is sufficient for complete clumping in the vast majority of positive cases. Lastly, and perhaps most important of all, the test is practically worthless if it is practised without a *control*. I always insist on a known positive blood and a known negative blood being examined with the serum of the case to be diagnosed. Only in this way can we have any assurance that the culture is reliable. Cultures occasionally go wrong, and will agglutinate with almost any serum. If the controls react unexpectedly, the culture must be condemned, and it is wise to destroy the stock from which it has been taken.

The dilution of the blood to 1 in 10, at least, before, in the process of mixing, it can come into contact with any bacilli, will prevent the occurrence of partial reactions.

The **macroscopic method** more generally used in laboratories has many advantages and depends on the sedimentation of the agglutinated masses to the bottom of a small test tube, the supernatant fluid in a positive case remaining clear while in negative cases a uniform turbidity persists. The test can be performed either with an emulsion of living bacilli or with a standard culture of bacilli killed by the addition of 0·1 per cent. of commercial formalin. The latter, the Oxford method, appears to me the simplest and gives, as it claims, a definite standard to work by. We have recently used it as a routine. A rack of fifteen small test tubes, five in each row, is employed, and one row is allotted to each of the three enteric micro-organisms. Dilutions to the required amounts, rising to 1-125 or 1-200 for instance, are

made in four of the tubes and the fifth is left as a control, with no serum added. The varying systems of obtaining the dilutions and the full technique of the tests will be found in any modern book on bacteriological methods. The tubes are placed in a water-bath at 55° C. for two hours, or left at room temperature for twenty-four, and the results are read off.

The standard cultures have the advantage of allowing the test to be always performed with a suspension of the same density giving comparable results. They are therefore particularly valuable when it is necessary to watch the curve of the agglutination titre, and make numerous examinations of the same serum at short intervals, say every four days. A single examination of the *reaction in inoculated persons* is of no use for diagnosis. Assuming the inoculation has been a triple one, the serum will agglutinate all three varieties of bacilli. If it has been with the bacillus typhosus alone, the agglutinins of that micro-organism will be present. Dreyer's method roughly consists in finding out the highest dilution in which agglutination takes place with each organism, and by successive examinations determining whether alterations in this titre occur or not. It is found, if one of the enteric fevers is present, that the titre for the corresponding organism rises sharply, reaches a maximum about the sixteenth day, and then shows a sharp fall which is most in evidence from the sixteenth to the twenty-fourth days, thereafter more slowly declining. The titre of the other organisms is not likely to show much decline during the comparatively short period for which the examinations last, and though a slight rise may correspond with that of the infecting organism it is not as a rule comparable with it. It may be said that, if blood cultures fail, this is the only way of making a diagnosis in the inoculated. The method has, however, been criticized by some workers and may perhaps be not quite so reliable as is claimed. Vincent has stated that by blood culture only can such a diagnosis be made. An interesting difficulty is that the titre will often rise as the result of any acute infection occurring in the inoculated. Before leaving this subject it should be noted that the A bacillus very frequently shows a much lower titre than the other two, and consequently it may, even after rising, give a lower figure than the others, although it is the infecting organism.

A phenomenon sometimes observed is agglutination in the higher dilutions, while the lower ones remain unaffected. This is caused by the action of substances known as *agglutinoids*.

In some instances the serum of an enteric patient who has not been inoculated will agglutinate all three micro-organisms to a greater or less degree. In such a case the reaction is said to be due to group agglutinins, and the agglutination curve should be studied to make a diagnosis. We have seen

also that the homologous agglutinins of typhus not infrequently agglutinate the bacillus typhosus.

As regards the **results** of the serum reaction, out of a series of 1,159 consecutive patients, all hospital cases under my own treatment, and all examined by the microscopic method, the serum of only eighteen gave questionable results. This is a margin of error of under 2 per cent. It must, of course, be understood, however, that the positive result was often considerably delayed, and the figures only refer to the final diagnosis. In all the cases which came to the post-mortem table, eighty-five in number, the test was proved to be accurate; those cases which, in life, had given a negative reaction, twenty-eight in all, showed no enteric lesions, whereas the remaining fifty-seven, all positive, presented characteristic intestinal changes. The diagnosis in the patients who survived, or on whom no necropsy was obtained, had to depend on clinical data, but even when, at the time of performing the test, the result caused surprise, the subsequent course of these cases was in accordance with the verdict of the reaction. Of the eighteen doubtful cases, some were doubtless instances of paratyphoid infection and thus failed to give a positive result.

The test may be positive in the first week of the fever, and is usually so in the second. In the third week, and after, it is rare not to find the reaction present. To sum up the *value of the reaction in diagnosis*, it may be said that a negative result in the first fortnight means little or nothing. If it is still negative in the third week there is an extremely strong presumption against a typhoid diagnosis. Should a negative reaction be still obtained after the third week is over, for practical purposes the idea of enteric fever may be dismissed. A positive reaction denotes that the patient either has the fever at the moment, has had it previously, and that probably at a comparatively recent date, or has been inoculated.

Other diagnostic reactions. Of these the most practicable is the *ophthalmic reaction* introduced by Chantemesse, on the lines of Calmette's tuberculin test. A drop of a specially prepared solution of typhoid toxin applied to the conjunctiva causes a slight inflammation if the case is one of enteric fever. I have not yet had the opportunity of practising this test, and after a limited experience of Calmette's reaction, in tubercular cases, I must confess to some hesitation in adopting it. It is sometimes easier to set up an inflammation than to check it.

The *typhoidin reaction* introduced by Gay and Force depends upon the evidence of localized hyper-susceptibility in the patient, and as at present performed consists of the intradermal injection of an alcohol and ether dried 'typhoidin' precipitated from a concentrated bouillon extract of

several strains of typhoid bacilli. The dose is the minimum effective one, 0·000005 grammes in 0·05 c.c. of 0·5 per cent. carbolated saline. A positive reaction consists in the presence after forty-eight hours of a definite indurated papule surrounded by a reddish areola of at least five millimetres. It apparently occurs too late to be of value in the diagnosis of the fever, but Gay believes it will prove of some use in determining the duration of immunity after inoculation. It has been observed in recovered cases of enteric fever of forty years' standing, and gives positive results in 75 per cent. of cases. I have as yet had no opportunity of trying it (p. 370).

PROGNOSIS AND MORTALITY. The severity of enteric fever differs much in different localities and in different epidemics. A mortality of from 7 to 17 per cent., taken all over, would probably be a fair estimate. Of my 1,700 cases, tabulated below, 168 or 9·8 per cent. died, the death-rate in the earlier cases of the series being higher than in those treated more recently. In my experience the type varies much from year to year, and therefore a general knowledge of the average mortality helps very little in estimating the chances of any particular group of cases. The fatality rate of the inoculated is very low.

Among the conditions, however, which affect prognosis, *age* takes a prominent place. In infants of under one year the mortality may be high, but, if these are excluded, the chances of children of under ten years of age are usually quite good. Thus of 511 children in this period of life the mortality was only 5·8 per cent., a not very formidable figure when compared with the case death-rate of such diseases as measles, scarlatina, or whooping-cough. The next quinquennial period seems even more favourable to the patient, only 3·6 per cent. of my cases having succumbed. This low mortality is no doubt partly explained by the fact that ulcerative accidents are relatively rare before the age of fifteen, and that hæmorrhage, when it occurs, is much less fatal. It is when the age of puberty is passed that enteric fever becomes really dangerous, 15·2 per cent. of my cases between the ages of fifteen and twenty years having terminated fatally, and this rate of mortality is maintained during the succeeding periods. The small numbers of older persons shown in my table no doubt give an entirely wrong impression of the severity of the disease. It is generally admitted that as age advances the chances of recovery become less.

Sex also influences prognosis. Females have a lower rate of mortality than males, my figures for the two sexes being 8·3 per cent. and 10·2 per cent. respectively. This, however, only seems to be the case after puberty, and depends, as does the low death-rate of children, on the relative immunity of women from ulcerative accidents. Between the ages of fifteen and forty.

no less than 17 per cent. of my male patients died, as against 12 per cent. of the women treated. It must be recollected, however, that, in outbreaks characterized by the severity rather of the toxic than of the ulcerative symptoms, the mortality of females may be as high or higher than that of males. Thus at Brisbane, before the cold bath treatment was introduced by Hare, the death-rate of women was 2 per cent. higher than that of men. This treatment, which has no effect on the incidence of ulcerative accidents, is most efficacious in combating toxæmia, and, as the result of its employment, the percentage mortality of females was found to be 3 per cent. lower than that of the other sex.

As regards other considerations which may affect prognosis, it is generally admitted that if the patient, previous to his infection, has been exposed to conditions which entail great privation and fatigue, the illness is likely to run a more serious course. Broadly speaking, enteric fever is a very serious disease for those engaged on active military service. On the other hand, it is quite possible that an attack of the fever is more dangerous to the overfed than to the underfed, the patient being less likely to enter on the disease with an overloaded bowel. Stout heavy patients seldom do as well as those who are of lighter weight, a point which I have also noticed

TABLE B

<i>Age Period.</i>	<i>Males.</i>		<i>Females.</i>		<i>Total.</i>		<i>Percentage Mortality.</i>
	<i>Cases.</i>	<i>Deaths.</i>	<i>Cases.</i>	<i>Deaths.</i>	<i>Cases.</i>	<i>Deaths.</i>	
0-1	0	0	0	0	0	0	—
1-2	6	1	3	0	9	1	11.1
2-3	7	0	6	0	13	0	—
3-4	13	1	17	2	30	3	10.1
4-5	32	2	18	1	50	3	6.0
5-10	212	10	197	13	409	23	5.6
10-15	192	6	164	7	356	13	3.6
15-20	95	15	82	12	177	27	15.2
20-25	113	22	98	11	211	33	15.6
25-30	89	18	63	8	152	26	17.1
30-40	111	16	88	9	199	25	12.5
40-50	39	7	36	2	75	9	12.0
50-60	11	5	5	0	16	5	31.2
60-70	0	0	3	0	3	0	—
<i>Totals</i>	920	103	780	65	1,700	168	9.8

Table showing age distribution and mortality of 1,700 cases. It, however, does not express accurately the tendency of the mortality to rise with age, a fact so generally noted. It includes all cases, no deduction for deaths occurring within twenty-four hours of admission having been made. Cases of paratyphoid are, however, excluded.

in typhus fever. Alcoholism is a serious disability with which to start an attack of enteric, and the presence of any old-standing disease, whether cardiac, renal, or pulmonary, adds much to the risks of the patient. It used to be held that to move a case, once diagnosed as typhoid, was very prejudicial to the chances of recovery, and I have certainly seen a patient arrive in hospital, bleeding profusely from the bowel, the hæmorrhage having occurred for the first time in the ambulance. But there can be little doubt that the risk has been much exaggerated, and Brownlee has shown conclusively, in the Glasgow City Hospital reports, that the distance from which a patient is removed to hospital has not the slightest effect on the mortality. There is really no reason why removal should not be perfectly safe in the first fortnight of the illness, and even after that time, provided a suitable ambulance is used, the risk should be infinitesimal.

The *appearance* and attitude of the patient may give us great assistance in prognosis. The usual expression of the enteric patient is apathetic, and the face pale with only a slight flush. But if the face is congested, the expression stupid, the pupils contracted, and the conjunctivæ pink, we may safely assume that the case is much more than averagely severe. Cyanosis is an extremely bad sign. The ease with which a patient can move himself in bed is often a good test of the degree of prostration from which he is suffering. In many instances the pulse may be very poor and the patient look extremely ill, yet, if he can turn himself on his side and change his position without assistance, there is always hope for him. Much more dangerously ill is the patient who, with perhaps a much better pulse, lies like a log on his back, unable to shift his position, and, if anything, tending to slip down from his pillow. We are sometimes apt, in our anxiety to note small details, to neglect to notice the patient himself, but I am convinced that, with a little experience, the medical man can learn as much from the look and decubitus as he can from the pulse and temperature.

Of the two latter the *pulse* is, without question, the most important as regards prognosis. So long as it remains below 110 the patient is likely to do well. In children and neurotic women a much higher rate need not cause any alarm, but, when the pulse of a male adult reaches 120, there is usually good reason for anxiety. Particularly is this the case if this acceleration is noticed in the first fortnight of the fever, when a pulse below 100 might reasonably be expected. It is unusual for a male adult, whose pulse has exceeded 130 for twenty-four hours, to survive, but some women may make good recoveries after several weeks' fever with such a rate, and in children the pulse is often extremely rapid and yet no harm results.

Irregularity is a bad sign, suggesting, as it does, changes in the cardiac muscle. Fortunately it is not a very frequent feature of the pulse in typhoid. Smallness and compressibility and excessive dirotism are also danger signals. The pulse at the wrist is not always a safe guide to the condition of the heart. Obliteration of the first sound, when the heart is auscultated, suggests great cardiac weakness and a very guarded prognosis, and yet this sign may be present when the pulse has not appeared to be particularly bad. On the other hand, a patient may have a wretched pulse, and yet the strength and character of the heart-sounds may remain quite satisfactory. The judicious administration of stimulants is usually called for in these cases, and our prognosis will be much influenced by their effect. If the patient responds to their use the outlook may yet be quite hopeful. If, on the other hand, no improvement follows, the danger is greater.

So long as the pulse remains relatively low there is not much need to worry over the height of the *temperature*. In many patients high fever seems to mean a good reaction, and we have seen that, in apyrexial typhoid, quite severe symptoms may be met with in conjunction with low temperatures. The character of the pyrexia, however, if not its actual level, may be of great assistance in prognosis. An absence of definite morning remission suggests a severe case and, in the third week especially, is associated in my mind with the probable occurrence of ulcerative accidents. At an earlier stage the outlook may not be so serious, and the appearance of good remissions in the third week may be taken as an encouraging sign, even if there is no suggestion as yet of a lysis. It must be remembered that, if we attempt to draw any deductions from the temperature curve, a four-hourly chart is absolutely necessary. Temperatures taken at 8 a.m. and 8 p.m. only may leave the impression that the pyrexia is running in a straight line, whereas, if observations are made at other times, it may be found that an excellent remission occurs at 4 a.m. or at noon. A marked fall of temperature may be to the advantage of the patient, or the reverse. It may mean the commencement of long swings down to normal, and this, of course, is most likely to be the case if the fall takes place at the usual hour for the patient's remission. But it may also mean that hæmorrhage or perforation has occurred, and this, again, is more probable if the drop is observed at an unusual time in the day. To come to a definite conclusion we have the pulse to assist us. Should it remain at its previous rate, or be actually increased instead of falling with the temperature, the suggestion is that the fall is not to the patient's advantage. High levels of pyrexia in the evening need not cause anxiety if the morning remission is good, and we have seen that, in some forms of lysis, the evening temperature may remain, as it

were fixed, at high levels, while the morning readings become gradually lower. In convalescence, in the same way, a rise in the evening is of little importance if the temperature is steadily normal or subnormal in the morning. Irregularity of temperature, however, in early convalescence is often noted in those cases which ultimately relapse, and therefore too much confidence that relapse will not occur should not be felt till the readings are steadily subnormal. The possibility also of a relapse occurring late, that is to say, considerably more than a fortnight after the original fever has subsided, must not be lost sight of.

As regards other symptoms presented by the patient, the existence of the *typhoid state* marks a more than averagely severe case, and the longer the condition lasts the more ominous is the outlook. Most deaths are due to profound toxæmia, and therefore such severe toxic symptoms as continuous muttering delirium, excessive subsultus tendinum, and, above all, aimless picking at the bedclothes must alway cause great anxiety. If, in addition to this group of symptoms, there is evidence of much *hypostatic pneumonia*, such as accelerated respiration and cyanosis, the prognosis becomes exceedingly grave. Mere incontinence of fæces and urine need not be regarded too seriously. I have often seen it at the commencement of the lysis, even when it had not previously manifested itself, and when the patient in all other respects was obviously better. Some delirium may be noticed at the same time, and it would appear that in such cases the patient's nervous system does not adapt itself well to the marked variations in the temperature level usually present at this time. Head symptoms in young patients, even when very severe and simulating meningitis, are not by any means incompatible with complete recovery. If the spinal fluid on lumbar puncture remains clear, true meningitis, except of the tubercular variety, may be excluded with confidence, and hope always remains. Drowsiness at all ages is, generally speaking, a good sign. The patient who sleeps through his fever, however severe his symptoms, usually recovers.

Although well-marked ulceration is, as a rule, associated with severe toxic symptoms, it must never be forgotten that hæmorrhage and perforation are liable to occur in patients, the course of whose fever has been previously most favourable. Thus, in the chart illustrating perforation (Fig. 38), it will be noticed that the pulse the day before the accident did not exceed 100, and the temperature variation was fully two degrees. It is particularly the ulcerative complications which make the prognosis of enteric fever so uncertain, and, however apparently mild a case is, it is well to be guarded. Severe *diarrhœa*, not yielding to appropriate dietetic treatment, is a very

dangerous complication, and even irritability of the lower bowel, with small but frequent motions, may by exhausting the patient add much to the risks of the case. *Meteorism*, if it becomes extreme, is one of the most intractable and fatal of the manifestations of the disease.

Hæmorrhage is not directly fatal in a large number of cases ; that is to say, it is seldom that a patient dies as the result of the actual bleeding. But my experience has been that its occurrence is very prejudicial to the chances of ultimate recovery. Of 132 patients who, at one time or another during the fever, had blood in their stools, no less than forty-nine, or 37 per cent., ultimately succumbed. In many cases death did not occur till a week or ten days after a moderate hæmorrhage, and it would appear that the patient, weakened by loss of blood, was unable to withstand the toxæmia. Hæmorrhage, moreover, must always be regarded as serious, because, if it occurs any time after the end of the second week, its presence implies well-marked ulceration. The possibility of a subsequent perforation is obviously greater in such a case. Twelve, or about 9 per cent., of my cases of hæmorrhage terminated fatally by perforation, which thus accounted for one quarter of the deaths following this accident. In children and women the risks are less than in men. Of seventeen cases of hæmorrhage in persons under fifteen years of age only one died, and the mortality for the female sex was 28 per cent. Occasionally when a large bleeding occurs, if the patient rallies from the shock he appears to be the better for the occurrence, but this is not to be counted on. Nevertheless, small hæmorrhages, whether repeated or not, have on the whole been more fatal in my experience. A more or less continuous oozing, as evidenced by the frequent presence of small dark clots in the stools, is of evil omen.

As regards *perforation*, the prognosis must depend purely on the results of the operation. It is difficult to state the exact odds against recovery, as many unsuccessful cases are never reported, but at the most favourable estimate they cannot be less than five to one, quite moderate enough to justify interference, since it must be assumed for practical purposes that the patient who is not given the advantage of surgical aid will infallibly die.

Intercurrent *complications* add much to the dangers of the case. Of twenty-six patients who suffered from pneumonia, nine, or more than one-third, died. The risks are probably less when the disease starts with a co-existing pneumonia than when the pulmonary condition declares itself later on in the fever. Chronic renal disease is also serious, as might be expected when the excretion of toxins is all-important. Laryngitis is very dangerous, and is usually associated with a particularly severe infection. Of the sequelæ of enteric fever it may be said that they rather delay recovery than cause

death. Thus thrombosis is seldom fatal, and the same applies to bone inflammations and to the 'typhoid spine'.

In about 4 per cent. of the fatal cases *sudden death* is said to terminate the case. I have only seen one instance of it, and in that case post-mortem examination was not allowed. Often, however, there appears to be little found after death to explain the accident, which has been attributed to a variety of causes, such as myocarditis, cerebral anæmia, and embolism. It is apt to occur in early convalescence, and in some instances, at least, is probably due to some slight exertion, such as sitting up in bed or straining at stool. The possibility of its occurrence emphasizes the necessity for carefully watching the patient even after all fever has subsided.

The prognosis in *relapse* is extremely good. However ill the patient looks, and however poor the pulse, I am always inclined to take a hopeful view. Curschmann has estimated the mortality at about 2·5 per cent., and probably this is a fair average. Of the ninety-five cases in my series only two terminated fatally, and these deaths are the only ones which I have witnessed in over 150 relapses. One of my cases, a girl, died at the commencement of a third relapse, the onset of which, as did that of the two others, coincided exactly with a menstrual period. It will be noticed, however, that in the chart shown (Fig. 44) the first fever lasted nearly four weeks, and the two relapses over three each. The interval, moreover, between them was extremely short, and this, if the relapse is severe, increases the probability of a fatal result. Intercurrent relapses, indeed, are often serious, and it would appear that a few days of complete apyrexia are most beneficial to the patient who has to undergo a relapse. While in my own experience many persons seem to be improved in their general health after an attack of enteric fever, it must be held as proved that they are, as a rule, left weakened in resistance to ordinary disease. Dublin, who has estimated the expectation of life in these individuals, finds that for three years after the fever more than twice as many of them die than would be expected at their time of life. Enteric fever, then, continues to take its toll for some time after the patient has nominally recovered.

TREATMENT. There are probably few medical subjects on which so much has been written as the treatment of enteric fever, and, in examining this very extensive literature, we are at once struck by the multiplicity and diversity of the methods recommended. But whether the patient is drugged or bathed, whether he is starved or fed, the general tendency of the infection is towards recovery, and the vast majority of cases terminate favourably. And, if the temperature charts of patients treated by the most diverse methods are examined, it will be found that the general curve of

the pyrexia remains practically the same in all cases. There is as yet no specific treatment for enteric fever, nothing that will abort or cut short the disease, although certain hopeful experiments have been made in the direction of securing an efficient serum or vaccine. Till, however, their value is fully established, we must content ourselves with putting the patient in as favourable a condition as possible to combat the toxæmia, and with

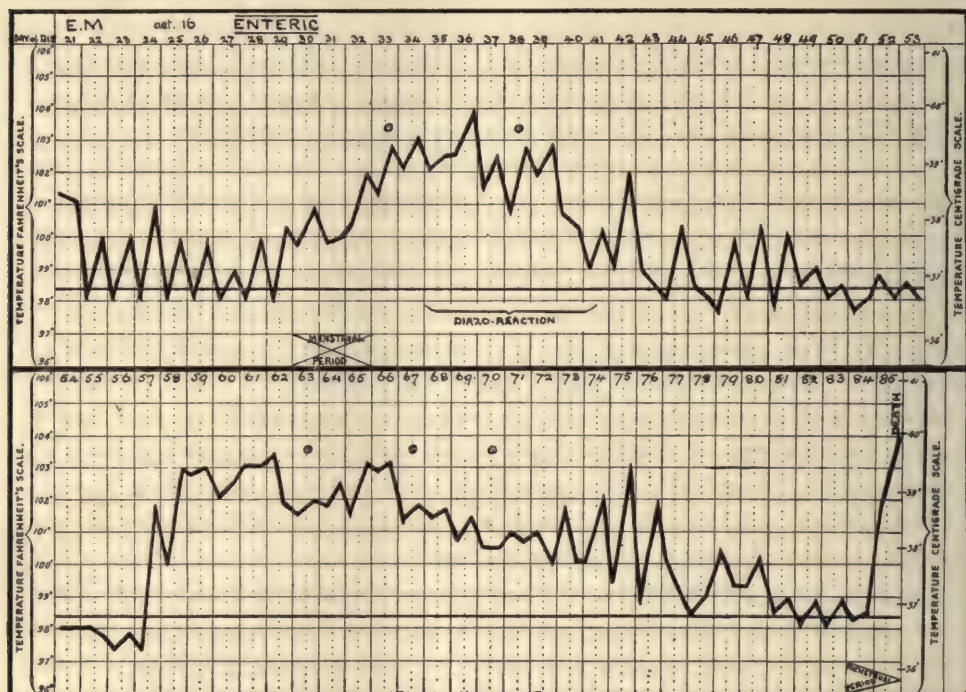


FIG. 44. A case of enteric fever with three relapses. The patient had previously suffered much from dysmenorrhœa. The first relapse coincided with symptoms suggesting menstrual difficulty—pelvic pain, vomiting, &c.—but no menstrual flow. The second relapse, twenty-eight days later, started with actual menstruation with much sickness and pain. After twenty-eight days more a third relapse commenced with menstrual symptoms. The patient vomited continuously and died in about twenty-four hours.

doing what we can to limit its ill effects. There is much to be learned from the study of the different methods of treatment in vogue, however contradictory to each other they may, at first sight, appear. We may, with advantage, first consider the general principles of management and dietetics, and, thereafter, examine in more or less detail some of the most important of the many systems of treatment which have been recommended.

Management. Sir Dyce Duckworth has said in a clinical lecture that the best treatment of enteric fever is a good doctor. I am almost

tempted to go further and to assert that the best treatment is a good nurse. In few diseases, indeed, is *nursing* so important as in enteric fever. Its long duration, its exhausting character, and the great importance of the early recognition of its ulcerative accidents, all combine to make the success of any treatment adopted largely dependent on the skill, devotion, and intelligence of the nurse employed. And when, in addition to this, we consider that diarrhoea and incontinence of urine are frequent symptoms, that the patient is often delirious and sometimes resistive, and that in hardly any other illness is care in dieting more important, we can readily comprehend what a heavy tax is laid on both the energy and conscience of the attending nurse.

In the first place, then, a trained nurse should be engaged, and, if possible, one who has had experience of typhoid nursing. The medical attendant, however, should in all cases supervise the nursing arrangements thoroughly, and satisfy himself that all is being done for his patient. The room should be as large as possible, and fresh air allowed to circulate freely through it, all unnecessary curtains and drapery being removed. The more fresh cool air that is supplied the better the patient will sleep, and the shorter will be his convalescence. The bed should be narrow and allow free access on both sides. A firm hair mattress is both more comfortable for the patient and assists the manipulations of the nurse. Water-beds, even in prolonged cases, are usually quite unnecessary. A draw-sheet, with a waterproof sheet below, should always lie under the patient's hips.

Once in bed the patient must be kept strictly in the recumbent position, and the bed-pan should always be used. Many patients are doubtless physically fit to use a night-stool, but to permit this is to allow unnecessary risks. The skin may be kept in good condition by the frequent use of the tepid sponge, which should be used systematically night and morning, and much more frequently in severe cases. When the patient is to be sponged he should lie in blankets provided for the purpose, and each limb should be thoroughly dried after the sponge has passed over it. The sponge should neither be dripping nor squeezed out, but should be thoroughly wet. If it is desired to lower temperature, however, a dripping sponge is no disadvantage, and the water may be cold or iced. The parts exposed to pressure should be rubbed with methylated spirit twice daily, after the morning and evening sponges, and in any parts which show redness a dusting powder of boracic acid and starch, with perhaps a little bismuth or zinc oxide added, may be freely applied. Some of our nurses, when the dependent parts are much reddened, have great faith in the use of zinc ointment, rubbed in with methylated spirit, a method which appears to avoid the caking of the

preparation on the skin. After each motion the skin of the buttocks and thighs must be carefully sponged, dried, and powdered.

The *toilet of the mouth* is a matter of great importance. In severe cases it may have to be cleaned every four hours. The cleaning may be done with cotton-wool swabs on metal sponge-holders, or perhaps more thoroughly and adequately with a piece of soft rag on the finger of the nurse. The swab or rag should also be used to apply some mildly antiseptic ointment to the mucous membranes of the mouth. Equal parts of boroglyceride and glycerine make a useful preparation, but I always use a prescription of Professor Wyllie's, one drachm of boracic acid to the ounce of vaseline, flavoured with 5 drops of oil of peppermint. In addition to this swabbing of the mucous membranes of the mouth and fauces, it may be not unnecessary to add that the more water a patient is given the better the condition of his tongue and mouth is likely to be. One of the most important, and also one of the most difficult, of the nurse's duties, will be to see that a delirious patient receives a sufficiency of fluid.

So long as a patient is able to lie on his side he should never be allowed to remain long on his back, and, if necessary, he must be propped with a pillow behind him into the required position. The side on which he lies should be changed at intervals, especially when he is awake. It is advisable, however, not to worry the patient who can only obtain adequate sleep on one side. Some lay stress on the advantage of the left lateral position, rather than the right, and this, theoretically, is certainly preferable, tending to prevent stagnation in the neighbourhood of the cæcum. But I must confess that I have never attempted to insist on this position. By turning patients, who are suffering from severe toxæmia, at frequent intervals much can be done to avoid hypostatic congestion of the lungs.

The medical attendant will make it his duty to examine daily the abdomen of the patient. It is only by this precaution that he can notice slight alterations in the amount of tumidity, which may be important in the diagnosis of a perforation, or which may have some bearing on the effects of any change in the diet. The stools also must be frequently inspected, attention being particularly paid to the presence or absence of blood, of sloughs, or of undigested particles of food, especially curds of milk. The condition of the mouth and tongue will enable him to satisfy himself as to whether they are being properly attended to, and as to the amount of fluids the patient is taking. An eye must be kept on the bladder, which should be frequently examined in delirious cases.

Diet. It is universally admitted that in no acute infectious disease must more care be exercised with regard to the diet than in enteric fever.

The conditions presented by this fever are such as to force upon the practitioner's attention various problems in connexion with the feeding of the patient. When we consider how extremely protracted the illness may be, and how enormous is the amount of tissue waste involved in the process, our tendency is to be liberal in the dietary with a view of maintaining the strength of the patient and shortening his convalescence. On the other hand, when we remember the state of the small intestine, often deeply ulcerated, always more or less impaired in its digestive power, we are inclined rather to cut down the supplies of nourishment to the lowest possible amount, in the fear lest, by giving too much, we may but aggravate the condition. The result is that the dietaries which have been recommended for enteric fever vary from what might be fairly described as a full diet to what might, without injustice, be termed no diet at all. Between these extremes there is an extraordinary choice of dietetic systems, all of which are claimed to have given admirable results.

The results obtained by systems very different in theory, but apparently equally successful in practice, almost lead us to the heretical conclusion that diet, after all, is not a matter of such supreme importance in this fever. Patients make good recoveries on large quantities of solid food. Others do equally well on a diet from which all solids are rigorously excluded, or which may be even limited to small quantities of water alone for days at a time. If any deduction is to be made from this, it is, I think, that the condition of the food when it reaches the small intestine is of much more importance than its condition when offered to the patient. The residuum left by milk may be, and often is, far more irritating to the intestine than the residuum of a mutton chop. Another point worth considering in this connexion is that, in many cases of enteric fever, the bowel is very slightly affected. Probably a considerable proportion of the patients who recover have but little ulceration, and of them it would be certainly fair to conclude that they would get through their fever whether their diet was solid or fluid.

The most reasonable course to take in prescribing a diet for a typhoid patient is, I think, to treat him as a patient and not as a case, and to modify the dietary according to his personal idiosyncrasies and the character of his illness. On the other hand, it is highly desirable to have some definite line of treatment, and the diet must necessarily be such as not to interfere in any way with the theory on which that treatment is based. It is my intention first to describe a dietary which may be used with advantage whether the patient is treated expectantly, with antiseptics, or with cold baths; secondly, to discuss the modifications which may be called for in

the presence of certain complications ; and, lastly, to briefly mention some of the special dietaries which have been suggested by various writers, and which seem to me to be worthy of notice. Diet, calculated on the scientific requirements of the patient according to its caloric value, as recommended by many American writers, will also be considered.

Diet for ordinary cases in the acute stage. The value of milk as a food in any fever is, of course, beyond all question, and it is still recognized by most authorities as the most suitable form of diet for cases of enteric fever. Still, if the greatest care is not taken, there are few foods which are capable of doing more harm. The famous epitaph of Graves has, perhaps, been responsible for a tendency to overfeed fever patients. Overfeeding, if the staple article of diet is milk, may be very dangerous, as, if more is ingested than the patient's alimentary system can adequately deal with, large masses of undigested curd are left to irritate the ileum and the lower bowel. The result is meteorism and diarrhoea, which are always dangerous and, too often, fatal. On the other hand, it is not enough to merely limit the amount of milk which is to be given in the twenty-four hours. Even moderate and reasonable quantities, given improperly, may cause much mischief. The most common error, one far too frequently met with, is to allow the milk to stand at the patient's bedside. As a result, it is used to quench his thirst, and small amounts are taken at very short intervals. Undigested milk is mixed with partly and completely digested milk in the stomach, and the whole mass may be passed on to the duodenum very imperfectly treated with the gastric juices. The consequence is that the stomach gets no rest, and the intestine is asked to deal with masses of curd. In such circumstances it is impossible to expect good results.

Rules for the administration of milk. Milk, however, still remains, in my opinion, far the best staple food for the typhoid patient, and all that is necessary to render its employment perfectly safe is to lay down sufficiently rigid rules for its administration. The first of these is that it is on no account to be used to quench the patient's thirst. Rather is it to be regarded as the solid part of his food, water being supplied freely when he requires it. Secondly, the milk must be supplied in measured quantities, and at regular intervals. Each supply should be looked upon as a separate meal. As regards the length of time between these meals, I am accustomed to make it two hours. In many cases, no doubt, a larger amount of milk every three hours would be equally satisfactory, and at night it will be often found advisable to prolong the intervals so as to disturb the sleep as little as possible. It would be imprudent, however, to leave the patient without nourishment for more than four hours, even at night. As regards

the amount of milk given, I am convinced that the power of milk digestion of the average patient has been much overrated. I never start a case on more than 3 ounces every two hours, that is to say, somewhat under two pints daily. It is seldom of advantage to increase this amount by much. Personally I make 4 ounces my maximum, and do not often exceed $3\frac{1}{2}$ ounces. Larger quantities are often very imperfectly digested.

The milk is always the better for being diluted, and for this purpose hot water may be added in the proportion of one to four, or one to three, of milk. The warmth of the mixture assists the digestion, which is also aided by the dilution, the curd being probably less firm. If more drastic methods of moving the bowels are objected to, fluid magnesia may be added to the water used as a diluent. Lime-water is also very useful in this connexion, should there be a tendency to diarrhœa.

Another rule of great importance is that the portion of milk must be consumed within a reasonable limit of time, certainly within a quarter of an hour. On no account is it to be allowed to stand at the bedside. It is very necessary that the stomach should have an adequate rest before the next meal.

The presence in the stools of undigested curd, whether in large masses or small flakes, proves that either more milk is being given than the digestion can tolerate, or that proper care is not being exercised in its administration. The deduction of half an ounce from the two-hourly allowance is often sufficient to cause a complete disappearance of curds from the motions, and, as a result, to check that tendency to looseness of the bowels which is so often occasioned by the presence of undigested food in the intestine. If it is found that milk is badly tolerated, even when given carefully, an admirable substitute may be found in whey.

Supplements to an exclusive milk diet. While many patients are sufficiently nourished by milk alone, it is advisable to supplement such a diet by the use of beef-tea, meat extracts, and similar preparations. As regards the first it is well to wait until the patient has been twenty-four hours under observation. Should diarrhœa be present, the use of hot beef-tea would only aggravate it; should there be blood in the stools, anything tending to loosen the bowels is to be deprecated. If, on the other hand, after a short period of observation it is found that there is no diarrhœa and that the condition of the stools is satisfactory, the use of one or other of the meat broths is of distinct advantage. A purely milk diet is terribly monotonous, and a reasonable allowance of chicken or beef tea is much appreciated by the patient. These preparations should be given well salted. They form, indeed, an admirable vehicle for the salt which is so much

craved for by patients who are kept upon an exclusively milk diet. Much of the hunger, in fact, which is so characteristic of enteric fever is probably due to the deprivation of salt which a strict milk régime entails. The first articles of food desired are usually those which have a salt flavour, such as ham, kippered herrings, and the like. This 'false appetite' often disappears completely if a sufficiency of salt is added to the chicken or beef tea. I prefer this to salting the patient's milk, which, however, may be done in moderation if it is considered undesirable to give the meat preparations. Taste is often so blunted in enteric fever that an amount of salt which would be nauseous to an individual in health is readily tolerated. Still it is necessary to take the greatest care not to disgust the patient with milk, if he is to depend upon it as his chief article of diet.

Value of beef-tea and similar preparations. It has been said above that the actual food value of beef or chicken tea is probably extremely small. They are much more useful as stimulants and hypnotics. Professor Wyllie, to whose teaching and example I owe this particular system of dieting, was accustomed, when consulting physician at the City Hospital, to recommend that the daily allowance of beef-tea, usually a pint, should be divided into three equal portions, the first of which, given at mid-day, broke the monotony of the constantly repeated milk, the second, given very hot at night, assisted the patient to get to sleep, and the third, given in the early hours of the morning as a stimulant, helped to tide him over the period of his greatest depression. I am certainly convinced that by a rational use of hot beef and chicken tea in this manner, hypnotics and alcoholic stimulants can often be dispensed with. The distinct laxative effect of strong beef-tea, moreover, is occasionally very useful in constipated cases.

Should there be much diarrhoea it may be found advantageous to make use of one of the many meat extracts which are nowadays available, or to employ raw meat juice. As a rule the former preparations are the most convenient. They should be given cold, and mixed with a little water. I usually prescribe bovinine, in the nutritive value of which I have a very firm belief. Valentine's meat juice is also admirably tolerated by patients with severe diarrhoea, and a very pleasant preparation is Brand's chicken jelly, which is the most agreeable to the patient of the three. There is a wide choice of these meat extracts, and the practitioner will do well to employ the one in which he has reason to feel most confidence, always provided of course that he is satisfied that it will not aggravate the diarrhoea.

Additions to the above diet in prolonged cases. While, in my experience, the average typhoid patient maintains his strength satisfactorily on the limited diet outlined above, in certain cases it will be found advisable to

supplement it. When the fever is very prolonged and there is excessive wasting, such substances as plasmon, somatose, sanatogen, and similar preparations may be added. Or maltine, a dessert-spoonful to each pint of milk, may be given to make up for the deficiency of carbohydrates in the diet. Half an egg beaten up in a little milk, with a teaspoonful or two of brandy added, may be administered twice in the twenty-four hours. Albumin water will also be found useful. A small amount of very well-boiled rice may be added to the patient's beef-tea, and jelly with wine or fruit flavourings may be safely employed to supplement the diet. If the patient fancies it, I see no objection to giving tablets of plain or milk chocolate. This greater liberality is also advisable in case of relapse, especially if the first attack has been at all protracted. Wasting is, of course, to be expected in every case of enteric fever, but it may unquestionably be allowed to go too far. Any of the above additions may also be made in cases where the hunger of the patient appears to remain unaffected by an increase in the amount of milk given, or by the addition of more salt to the food allowed. This is particularly the case during the stage of defervescence.

Indications for increasing the diet in convalescence. Assuming that a patient has satisfactorily passed through his fever, and that the temperature is approaching the normal line, when is the first increase of diet to be made? Much must depend upon the circumstances of the individual case. Unless he is really hungry there is no particular advantage in making any addition to the diet till the temperature is steadily normal. By 'real hunger' is to be understood a genuine craving for food; that is to say, it is not enough for the patient to reply that he is hungry, when asked. He must volunteer the information himself. If his hunger is real, and all precautions to satisfy a 'false appetite' have already been taken, some addition to his food may be allowed when his temperature is normal in the mornings, the evening readings being disregarded. Should his diet, up to this point, have consisted exclusively of milk and meat broths, with the few extras that may have been permitted in prolonged cases, it is obvious that, before he is allowed solid food, he must be content with semi-solids and 'sloppy' materials. Benger's food, or boiled bread and milk, is usually my first addition, and the effect of even this slight increase of diet upon the patient must be carefully noted. If the morning temperature remains normal, the bread and milk is continued for two or three days, the amount given being gradually increased, and a little well-boiled oat-flour porridge being added to give variety. By this time the evening temperature has also, frequently, settled, but, even if not, another increase may be safely tried, always provided there has been no rise above normal in the mornings. At this stage the first solids may be

given, a sponge-biscuit, or a small amount of light sponge-cake, being a quite suitable substance to experiment with. If this is tolerated I am accustomed to allow next day a very small quantity of white fish. This should be boiled or steamed, and all skin should be carefully removed. The best fish for this purpose is whiting, but in hospital practice fresh haddock forms an admirable substitute. A very thin finger of bread, from which all crust has been cut, may be given with the fish. On the following day, always assuming that the morning temperature is steadily normal, a little thin bread and butter may be permitted at breakfast and tea time, the patient still receiving a reasonable quantity of milk at intervals, and beef and chicken tea being continued exactly as before. For three or four days this diet may be continued, the amount of food given being cautiously increased, and such additions as a little baked custard pudding with stewed fruit, or some well-boiled milk pudding may be allowed. Should the morning temperature rise above normal, it is wise to go back to the fluid diet at once, until, at least, the cause of the pyrexia has been ascertained. It is rarely necessary to make much modification in the diet for pyrexia depending upon such conditions as constipation, otitis media, or thrombosis.

Should, however, the addition of solids to the dietary leave the temperature quite undisturbed, after a few days of steady increase in the amount of food given, a further step might be taken, and the patient allowed a little of the breast or wing of a chicken. My patients, as a rule, receive this from three to five days after their first allowance of fish. With the chicken may be given a little mashed potato, which indeed may be quite safely given when the diet is limited to fish. Chicken having been allowed, there is no advantage in a further increase until all chance of relapse has disappeared, after which (say a fortnight's completely normal temperature) there is no reason why meat should not be permitted in moderation. In moderation, indeed, success in the dieting of an enteric patient usually lies. As much variety of food as possible should be given, but at first only in small amounts.

It will be noticed that very little attention is paid to the evening temperature, which cannot be regarded as a reliable guide. We have seen elsewhere that the high spiking temperature of convalescence is sometimes due to inanition. The effect of disregarding such pyrexia is illustrated in the chart on p. 280 (Fig. 36). When the temperature, however, is normal, both morning and evening, rather than subnormal, there is always a fair chance of relapse, and it appears reasonable, while making the usual additions to the food, not to attempt to overfeed.

As to the *effect of diet on the occurrence of relapses* it is, I think, very problematical. An injudicious addition to the diet may cause a rise of

temperature most undoubtedly, but such a rise will subside on the removal of the cause. In some patients, especially those who have been restricted to fluid diet in early convalescence, the first solid food occasionally causes an elevation of temperature, probably from some reflex cause. To others, again, the first allowance of solids is such an event that their excitement is quite sufficient to account for the subsequent pyrexia. True relapses occur equally frequently in cases which have been rigidly dieted as in those which are fed liberally. This is shown by the fact that the percentage of relapses in a series of 397 consecutive cases of enteric fever, which were dieted less liberally and less early in convalescence than is suggested above, was 5.79, whereas out of a subsequent series of 758 cases, the diet in which was on the exact lines I have indicated, only 3.95 per cent. relapsed. These figures go far to show that relapses are, at least, not increased in number by early and liberal feeding in convalescence, as do also those of Kinnicutt, which will be found quoted on a later page.

Drink of the patient during the fever. In the acute stage of the fever we have seen that the patient is restricted to a fluid diet. But it was emphasized that milk is to be regarded as the solid part of the patient's food and must be given in regular meals. It cannot, then, be used to quench the thirst of the patient. For the latter purpose there is nothing more suitable than cold water, which must be always kept standing at the bedside, so that the invalid can help himself. The greatest attention must be paid by the nurse to unconscious and delirious patients, and water should be offered to them frequently, and forced upon them when necessary. Much good, in fact, may be done by forcing large quantities of water upon patients. Three to four pints daily, in addition to the fluid diet already prescribed, should be a minimum allowance. As regards greater amounts than this, we will have occasion to allude to the systematic administration of large quantities of water on a later page (p. 360).

I cannot approve of the common custom of allowing aerated waters, usually in conjunction with milk, to the typhoid patient. They are most liable to cause distension, always a condition to be scrupulously avoided. If the patient dislikes cold water, a lemon acid drink may be prescribed, composed of a few drops of dilute hydrochloric acid and syrup of lemons, very freely diluted, but retaining a sufficient taste of acid to be refreshing to the patient. It is always easier to induce the patient to drink something which has a definite flavour, and, moreover, hydrochloric acid has a certain classical reputation in the therapeutics of fever, and has been recommended as a mild febrifuge both by Murchison and Fagge.

Under ordinary circumstances it is only reasonable to allow tea to patients

who appreciate it. A cup of tea, given to a female patient at about four o'clock in the afternoon, is usually rather good for her than otherwise. It is an event in the dreary monotony of the day, and has, as a rule, a good effect mentally. It is almost needless to add that it should be freshly infused, not too strong, and given with plenty of milk. The only contra-indication is marked insomnia, although it is very doubtful if tea has much effect in keeping awake those who are thoroughly accustomed to it. Cocoa may also be given to those who like it, and it may form an admirable means of administering a sufficiency of milk to patients who take the latter badly.

Modifications of diet to meet various conditions. In a case in which care has been taken as regards the diet it is unusual for severe *diarrhœa* to occur. On the contrary, this symptom usually subsides when the patient is dieted suitably. Occasionally, however, severe *diarrhœa* may persist, or may, indeed, even supervene in a properly dieted case. If the patient is having beef or chicken tea these should be at once stopped. If any substitute is required, raw meat juice, or one of the meat extracts, may be given cold. The milk must be boiled, and diluted with lime-water instead of with water alone. If this is insufficient to check the condition, the amount of milk should be considerably reduced, and it may be peptonized or pancreatized. If whisky is being given it should be withdrawn and brandy substituted. Again, in cases of *meteorism*, much may be done by reducing the quantity of milk allowed and by peptonizing it. The desirability of avoiding aerated waters has been already alluded to. When *constipation* is troublesome, the addition of beef-tea, made strong, if it is not already being given, will often have the desired effect. A little fluid magnesia may also be added to the milk, if necessary. The question of diet, when such accidents as hæmorrhage or perforation have occurred, will be considered when the treatment of those conditions is discussed. Of other conditions likely to complicate the course of the fever, persistent *vomiting* may call for a modification in the diet. In this case peptonizing the milk may be first tried, and, if that fails, iced albumin water is sometimes tolerated. Raw meat juice is taken well by some patients when the stomach will not tolerate milk. As a last resort rectal feeding may be necessary, but this is not applicable to cases in which there is also *diarrhœa*. In convalescence, such conditions as thrombosis, periostitis, and skin abscesses call rather for an increase than a diminution in the diet, always provided that the pyrexia is not so decided as to seriously interfere with gastric digestion.

The above lines of dieting have answered well in my experience, and it may be mentioned that a very similar method, with milk as the staple food, appears to be that generally adopted in France. The system, then, will be

found useful especially by those who, having only a limited experience of enteric fever, are anxious to adopt a perfectly safe plan of dieting. Modifications will be necessary in the case of individuals who may refuse not only milk but even soft solids or solids. I had some years ago a German seaman under my care who refused everything offered him except milk chocolate and lager beer, on which somewhat bizarre combination he lived entirely for a fortnight and made a good recovery. I quote this extreme instance to point the moral that it is always worth while to consider personal idiosyncrasies. It is also well to remember that the more strictly a patient is dieted the more he is liable to suffer from any irregularity in his diet. The importance of watching the stools and the abdomen, and of modifying the diet accordingly, has already been emphasized.

Diet for children. It is obvious that, except in the youngest children, the diet, as recommended for adults, can in most cases be given. Any modification of it should be in the direction of caution rather than liberality. Children tolerate milk and thrive on milk better than adults, and a milk diet in the acute stage, gradually increased to soft solids in convalescence, and to solids a little later than is recommended for adults, will in most instances be found satisfactory.

As has been already stated, other methods of dieting, chiefly on more liberal lines, have been strongly advocated, and the success which they have met with in the hands of competent physicians has been such as to demand our most earnest attention. It has been thought well, therefore, to mention some of the most important. Their study is instructive, as, when dealing with patients who cannot tolerate milk, we are often at a loss to know what may be safely substituted for it.

Liberal feeding in enteric fever. There is no doubt that, theoretically, there is much to be gained by giving a liberal and varied diet. The bowel-wall of a patient who has succumbed to enteric fever is often found at the autopsy to be extremely thin. Is it possible that, by unduly restricting the food supply of the patient, we are weakening the resistance of his bowel-wall to the ulcerative process? I am convinced that the use of solid food early in convalescence does much to shorten the duration of the case. Does the more liberal supply of food at this period help to promote the healing process in the ulcerated intestine as well as to repair the waste caused by the fever? That it prevents to some extent such sequelæ as periostitis, abscesses, and otitis media is, at least, probable. If such additions are justifiable from the moment the temperature touches normal, would they not be equally so at an earlier period, say at the commencement of the lysis, when the patient is beginning to show signs of returning appetite?

The only argument against the giving of solid food throughout the fever, say the advocates of a mixed diet, is the inability of the patient to take it. Other objections are mainly theoretical, such as that it is liable to cause hæmorrhage or perforation, or that it increases the tendency to relapse. We have seen above that solid food, early in convalescence, has little or no influence on the frequency of relapses. There is, therefore, no reason to believe that relapses would be more frequent in cases which have been treated with a mixed diet during the acute stage.

Theoretical objections to milk. On the other hand, although most physicians will agree that milk is the most convenient food to use during the acute stage of the fever, it is not altogether an ideal diet. It contains more fat than necessary, probably too little protein, and it is certainly deficient in carbohydrates. It is said, and no doubt from the laboratory point of view the statement is correct, that, to make good the waste caused by the increased metabolism in such a fever as enteric, it is necessary for the patient to take 8 ounces of milk every two hours. Such an amount is obviously impossible, and therefore, if the waste is to be considered, the milk should be supplemented by other articles of food.

It has been suggested that the deficiency of milk in iron salts is probably responsible for the prolonged anæmia which often follows enteric fever. Wright, moreover, has pointed out that the increased coagulability of the blood, which assists the occurrence of such a sequela as thrombosis, is due in all probability to a prolonged milk diet. Further, it is advanced that the mastication of solid food in the mouth excites reflexes which aid digestion, and that milk which becomes a semi-solid in the stomach has all the disadvantages and none of the advantages of a solid food. It must be admitted that the undigested residuum of milk may be extremely irritating to the intestine, but much of this difficulty can be obviated by giving the milk properly. Lastly, it has been asserted that milk acts as an admirable culture medium for the typhoid and intestinal micro-organisms, and that its employment should be limited on that account. This objection is more valid than the identical one which has been raised with regard to the use of beef-tea, which surely can leave practically no residuum for the benefit of the intestinal germs.

Suggestions for dieting with solid food in the acute stage. No account of the dietetics of enteric fever can be considered adequate without some reference to the interesting dietary suggested by the Russian physician Bushuyev. His published results did much to stimulate experiments in the direction of a more liberal diet, especially in America, and if few have followed his system in its completeness, many have modified it and been satisfied with

the results obtained. His treatment is to give solid food to all who can take it from the moment they come under observation. Meat, bread, and boiled eggs, hard or soft, are all allowed. In a series of 398 patients only four suffered from hæmorrhage and one from perforation. The mortality of the cases was 8·2 per cent. The Russian physician is convinced that once a patient's interest can be stimulated in his diet, his general condition is at once improved. The detailed dietary which he gives is quite sufficient to nourish a healthy man in full exercise.

In England, Barrs, whose results were published a year earlier than those of Bushuyev, while believing equally in the value of solid food, takes a less pronounced and more rational view of the question. The appetite of the patient, once the physician has satisfied himself that the hunger is really genuine, is to be regarded as the indication for solid food. Barrs considers, from a study of his cases, that there is no reason to believe that diarrhœa is rendered worse by a liberal diet, or that perforation occurs more frequently in liberally fed patients. Meat and bread are allowed throughout the acute stage. The meat is usually minced at first, as otherwise it is difficult to take unless the patient is permitted to sit up. Recently Galambos has reported excellent results on a diet of chicken, potato, eggs, brains, ham, &c., in a series of 2,000 patients, and found the number of relapses was much reduced.

Soft solids and mixed diet in the acute stage. Shattuck, at the Massachusetts General Hospital, feeds his typhoid patients on the following lines:—

1. Milk diluted with lime-water or aerated water and sometimes salted, peptonized milk, cream and water, milk with white of egg, buttermilk, koumiss, milk whey, milk with tea, coffee, or cocoa.

2. Soups, both meat and vegetable, carefully strained and thickened with arrowroot, flour, milk, egg, or barley.

3. Horlick's or Mellin's food, malted milk, carnipectone, bovine, and somatose.

4. Beef juice.

5. Gruels of strained corn-meal, crackers, flour. Barley-water, toast-water, albumin water with lemon-juice.

6. Ice-cream.

7. Eggs, soft boiled or raw, egg nogg.

8. Finely minced lean meat, scraped beef. The soft part of raw oysters. Soft crackers, with milk or broth. Soft puddings, without raisins. Blanc-mange, wine jelly, apple sauce, and macaroni.

This diet may be accepted as that favoured by American physicians, who believe in varied feeding. Manges, Fitz, and Kinnicutt have all had

success with dietaries very much upon the above lines. Vaquez, in France, has also had good results with a similar diet. Marsden, at the Manchester Fever Hospital, allowed bread and milk, custard, and minced meat to those patients who were hungry, and gave fish in many instances before the temperature was normal. His conclusion was that with such a diet there is more rapid recovery, less risk of surreptitious feeding, and a lessened tendency to asthenic complications. His hæmorrhage rate was low, only 3 per cent., and of 200 patients not one perforated.

My own experience of liberal feeding throughout the fever is not extensive, but I certainly saw no harm result from the use during the acute stage of milk puddings, bread and milk, and beef-tea thickened with well-boiled rice, the diet which was given by my predecessor at the City Hospital. And during the stage of defervescence, and in early convalescence, we frequently allowed potatoes mashed in gravy with apparently very good results. All these foods helped to supply the carbohydrates in which milk is so deficient. Fish, too, was often given before the temperature was normal. A chart showing the diet and its effect in one of these cases is appended (Fig. 45). At present, however, I prefer a more rigid diet in the acute stage, and to postpone semi-solids to the period of early convalescence. The interesting figures published by Kinnicutt, on the other hand, go far to prove that it is quite safe to give a liberal dietary. He has collected records of 4,654 cases treated with fluid, and of 733 with liberal, diet, and the results are as follows :

<i>Cases.</i>		<i>Relapses per cent.</i>	<i>Hæmorrhages per cent.</i>	<i>Perforations per cent.</i>	<i>Mortality per cent.</i>
On liberal diet	733	11·38	4·77	1·36	9·47
On fluid diet	4,654	10·89	8·83	2·40	10·55

It is, of course, difficult to draw conclusions from statistics of this sort, but the greatest care has been taken by Kinnicutt that the test should be a fair one. The most interesting feature is the larger number of ulcerative accidents in the second group. The question again arises, how far does a low diet, by starving the bowel walls, help to increase rather than limit the process of ulceration ?

Scientific dieting. Although, no doubt, the diets already mentioned are founded upon theoretical considerations, which may have a scientific basis, they are mainly empirical. It is only natural that certain workers, impressed by the enormous destruction of protein in this fever, and the evident loss of weight, should endeavour to devise a dietary which should

prevent excessive waste. In this connexion we owe much to Coleman, who has made very valuable and interesting observations on the subject, and has proved that with appropriate dieting a patient can maintain, or actually increase, his weight during an attack of the fever. The loss of protein, regarded as of most importance, may be due to under-feeding, to pyrexia itself, and to toxic destruction as the result of infection with micro-organisms, and it would appear that the first of these factors is the most simple to deal with. Coleman found that a *high calory diet* will maintain fever patients in weight equilibrium during the whole course of their illness, and his charts show that 4,000 to 5,500 calories can be given daily with good effect, an amount in some instances rising to over ninety calories per kilogramme of body weight. The diet recommended consists of a liberal supply of milk, cream, butter, eggs, and lactose. The last-named is important, as it seems now to be generally agreed that, provided enough protein be supplied for daily needs, the loss of nitrogen is prevented by a diet rich in carbohydrates, and milk sugar is in many ways more suitable than the starches.

Meara, in his useful book on the treatment of infectious diseases, recommends 3,000 calories in the early weeks, to be increased later according to the wish and capacity of the patient. He suggests 70 to 90 grammes of protein, carbohydrates as the mainstay, and fats fairly liberally. Milk remains the basis of the dietary, 2 to 4 pints daily, one glass of eight ounces equalling 160 calories. This can be given enriched with cream and lactose, e. g.

one glass containing milk 7 ounces, 140 calories

„ cream 1 ounce, 50 „

„ lactose $\frac{1}{2}$ ounce, 60 „

equals 250 „

or one glass containing milk 6 ounces, 120 calories

„ cream 2 ounces, 100 „

„ lactose 1 ounce, 120 „

equals 340 „

It is easy to see how the amounts may be adjusted as required. To this diet from four to six eggs (each 80 calories), may be added daily, and given either raw, soft-boiled, or in custard. Bread (one slice of $1\frac{1}{4}$ ounces equals 100 calories) is given either as toast, milk toast, bread and milk, or bread and butter. Of other foodstuffs, two-fifths of an ounce of butter equals 100 calories, as do also a heaped tablespoonful of rice, or a medium-sized baked potato.

I must confess to not having tried a diet calculated on these lines, but it seems well adapted for the purpose, if perhaps a little excessive from my own point of view. The enteric patient regains weight so rapidly in early convalescence that even a marked loss during the fever does not appear to me to have the importance attributed to it. I have often found cream very useful, but it is not every patient who takes it well.

The empty bowel theory. Attention has been recently called by Ewart to the advantages of a diet which contains little or no residuum. The object is to give plenty of food to the patients, but to dispense with the fæces so far as is possible. It is obvious that there are many advantages in such a method. There should be an absence of any irritating residue which might increase the ulcerative process, and Ewart hints that, just as we have learned that phagedenic chancre and hospital gangrene are no longer held to be normal developments in pathology, so we may yet discover that typhoid ulceration is a preventable condition. That it may be so is, indeed, very probable, but, so far as regards hospital patients, the mischief will have usually commenced before they come under observation. Any diet, however, which claims to limit the severity of the process demands careful consideration, and the dietary outlined by Ewart contains many interesting and valuable suggestions.

The staple food is whey, given in quantities of from $2\frac{1}{2}$ to 4 pints in the twenty-four hours. This, it may be remarked, is always worth trying when a patient cannot digest milk, however carefully administered. Ewart adds from 10 to 15 grains of common salt to each half pint with a view of correcting the deficiency in mineral salts which an ordinary milk diet entails. He advises that the deficiency in phosphates should be made up by giving periodical doses of one of the medicinal syrups. Sugar is also added to the whey, being useful as a food and leaving no residuum. The salted whey alone should be given for the first two or three days until any meteorism has subsided. When this is the case and the stools are satisfactory, the sugar may be given. Next white of egg is added to the whey, which is then peptonized. This addition is made to secure sufficient nitrogenous material. Then cream, one ounce daily, either added to the whey or given alone, is permitted in order to make up for the deficiency of fats. Thereafter, fruit jellies, especially apple jelly, and vegetable soups are allowed. The meat preparations are not recommended. The yolk of one egg is given daily in divided portions. Clarified honey or maltine is useful, and forms a valuable addition to the supply of carbohydrates. Such a diet is certainly likely to leave little or no residuum, and from a practical point of view may be cordially recommended.

An *empty bowel* can also be secured by methods approaching to starvation. Queirolo has recommended that the feeding should be entirely rectal. Provided that the bowel of a patient so treated is first emptied by a dose of calomel or other suitable purgative, such a method of dieting should, at least, secure complete rest for the affected parts, and absolutely exclude the possibility of fermenting masses of partly digested material lying in the gut. The nutritive value of rectal feeding is, however, so limited that the system may fairly be regarded as treatment by starvation.

Similar in its objects and effects is the method suggested by Williams, who, believing that the exhausting diarrhoea of the fever is entirely due to improper feeding, endeavours to secure that the intestine shall, as far as possible, remain empty. Water alone is allowed in severe cases, sometimes for days at a time, and he regards half a pint of milk in the twenty-four hours as a liberal diet, seldom, apparently, exceeding this amount until the temperature is normal. The method seems drastic, but I have reason to know that the patients do remarkably well. I have often marvelled at

the amount of starvation which a typhoid patient can safely tolerate after a hæmorrhage, and it is only rational to suppose that, before the appearance of such a depressing complication, the deprivation would be still better supported.

The theoretical objection to such low diets is, that if ulceration has already started, they would give the intestinal lesions only a poor chance of repair; on the other hand, it is possible that the absence of irritation goes far to counterbalance this defect, especially as the patients seem to tolerate the starvation so admirably. If plenty of water were supplied, this would be more easily understood, but some of Williams's patients were

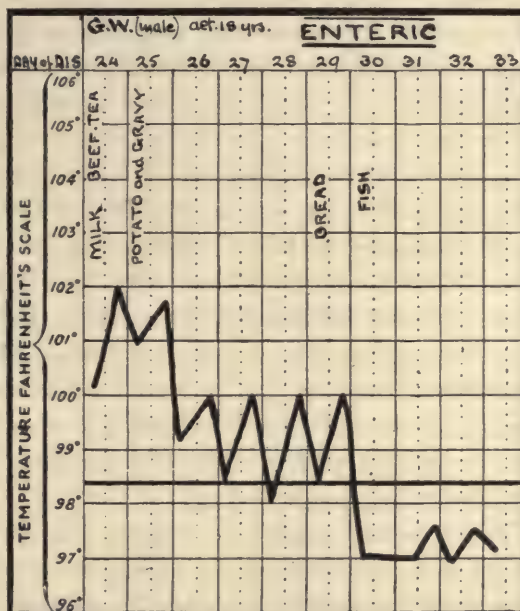


FIG. 45. To illustrate the favourable effect sometimes exercised on the temperature by the addition of soft solids and solids to a purely fluid diet. See also Fig. 36.

limited, for a time at least, to one pint of water per diem, which seems a most inadequate amount.

General conclusions as to diet. Enough has been said to show that the practitioner has a wide choice of dietaries for typhoid patients. Each system has something in its favour, and it is by the judicious application of the suggestions which we gather from each that we are likely to obtain the most satisfactory results. Thus, while following the rule that safety usually lies in moderation, and that extremes both in the direction of starvation and of liberal feeding may be with advantage avoided, we may, not infrequently, be confronted with cases in which the complete stoppage of all food substances on the one hand, or the early administration of solid food on the other, may do much to secure the recovery of the patient. My own view is that a fluid diet, consisting chiefly of milk, as indicated in the first part of this section, is the safest, and in the long run the most advantageous; in the acute stage of the fever, and that this diet should be rapidly increased in the early days of convalescence, due care being exercised in watching the effect of each addition. I believe that, if milk is properly given, it is well tolerated by the vast majority of cases, and that milk-free diets are only necessary in exceptional circumstances. I can see no benefit whatever in starving patients with practically normal temperatures, clean tongues, and good appetites, and my experience has been that solid food can be supplied with considerable liberality, and without risk, in the early convalescence of enteric fever.

Treatment: expectant. Many practitioners having adopted a particular diet are satisfied for the rest to treat the patient on expectant lines, in other words, to watch the progress of the case and only interfere when particular symptoms become troublesome. There is much to be said for this attitude. We cannot abort the disease, and more harm has been done by meddlesome interference than by the watching policy. I am inclined to recommend this expectant symptomatic method for those with small experience of the fever. Having dieted the case appropriately, nothing further need be done unless complications arise. Should some systematic drug administration be thought desirable, a suitable antiseptic, such as naphthol β or cinnamon oil, may be given in moderate doses. Further information about these drugs will be found under the head of Antiseptic Treatment (p. 356). The practitioner will often find it convenient to employ some drug, and in such circumstances he may feel assured that the antiseptic remedies named will do no harm.

It will be convenient here to make more suggestions as to how the different conditions which complicate the fever may best be treated. Having

done this we may turn our attention to systematic methods of treatment, which the practitioner may ultimately adopt in preference to the expectant method. The first question which is likely to trouble him is the regulation of the bowels. *Constipation* is a much more common feature of enteric fever than is generally supposed, and it is highly desirable that the patient should have at least one motion daily. We have already seen that the addition of one or two teaspoonfuls of fluid magnesia to one of the feeds of milk will often correct a slight degree of constipation. If this fails, the administration of a drachm to a drachm and a half of castor oil every evening is sometimes effectual. A simple enema, with a moderate amount of soap, should be occasionally given, and helps much to prevent meteorism. It may also not be out of place to add that most authorities agree that a dose of from 3 to 5 grains of calomel is useful to clear the bowel at the time the patient first comes under observation. *Diarrhoea* is best dealt with by modifying the diet, and, if curds are in the stools, the milk should be cut down, or whey substituted (see p. 337). - Occasionally, in spite of the greatest care in dieting, the diarrhoea persists. It is usually worth while to try an antiseptic drug in such cases, and the systematic administration of perchloride of mercury, naphthol, or guaiacol carbonate, for a few days may sometimes be of advantage. Irrigation of the large intestine with hot water, as described below (p. 359), is also very useful in this connexion. When the patient is losing his night's rest on account of frequent unsatisfactory little motions, a 5-grain Dover's powder overnight is a good prescription, or a starch and opium enema may be of service.

If *meteorism* occurs, the diet, again, must first be looked to. Enemata of hot water or small irrigations, frequently repeated, should be tried, and turpentine stupes may be laid on the abdomen. Turpentine, administered internally in 20-drop doses every two or four hours, is often efficacious, as are perchloride of mercury and other antiseptic drugs. The condition, however, if severe, is extremely intractable, and occasionally it is impossible to hold it in check. On two or three occasions I have been reduced to puncturing the abdomen with an ordinary antitoxin needle, but, though temporary relief is sometimes given, much cannot be hoped for by this method, which can only be considered justifiable in desperate cases with embarrassed heart's action.

There is some diversity of opinion as to the most advisable method of dealing with *hæmorrhage*. My own practice is to endeavour to put the bowel at rest, firstly by the withholding of all nourishment, and secondly by the administration of opium. By this method it is reasonable to expect that the natural arrest of hæmorrhage can be best encouraged. No food

or water is given by the mouth for from twelve to twenty-four hours after the accident, and, then, if no further bleeding has occurred, teaspoonfuls of bovine in iced water are cautiously allowed, at two-hourly intervals. Twelve or twenty-four hours later, again, dessert-spoonfuls of diluted or peptonized milk may be added, and, no further hæmorrhage occurring, the amount of milk may be gradually increased till the amount permitted before the appearance of the complication is reached. Not only does the administration of opium check the peristalsis and immobilize the patient himself, but it also prevents the latter being unduly conscious of the withdrawal of both his nourishment and his water. Two objections to its use, however, are urged. Firstly, if there is any tendency to meteorism, the paralysis of the intestine aggravates that dangerous complication. Secondly, should the patient be so unfortunate as to perforate, the signs of that condition, so important to recognize early, are liable to be completely masked. As regards the first of these objections, it may in some circumstances be a serious one, but the systematic use of turpentine, which is, perhaps, the most satisfactory drug to employ for hæmorrhage, does much to obviate the risk. The second objection is, in my opinion, more theoretical than practical. Of 132 patients who suffered from hæmorrhage, only twelve subsequently perforated, and in only two or three of these did perforation follow hæmorrhage so closely that it occurred before the patient was free from the influence of opium, which it is rarely necessary to maintain for more than three days. If opium is usually effective in controlling hæmorrhage, as I believe, are we to deny a bleeding patient its benefits, for fear he should subsequently be one of the 2 per cent. who perforate shortly after the hæmorrhage? As regards the administration of the drug, I prefer Dover's powder to any other preparation. A 5-grain powder, repeated in from one to two hours, if the patient is not sleeping, and thereafter every four or six hours for the first two days, has, on the whole, been more satisfactory in my hands than the hypodermic injection of morphia. The latter, however, may be first given, for the sake of its rapid action, if the bleeding is very profuse. Some patients, again, may obtain most benefit from the use of morphia suppositories. If after two days there has been no movement of the bowels, or no fresh blood in any stool that may have been passed, the opium may be withheld, and if, in spite of this, the bowels do not move, an olive-oil enema may be given on the fourth day. When the hæmorrhage is trivial, opium is probably unnecessary, or may be continued for twelve or twenty-four hours only. Of other drugs, turpentine in 10 or 20-minim doses, or tannalbin in doses of 15 grains, four-hourly, will be found most reliable. My experience with ergotine has not been very happy, and the

same applies to adrenalin and to injections of horse serum. I have used calcium chloride, but the work of Addis casts grave doubts upon its efficacy in increasing the coagulability of the blood. The application of ice to the abdomen is widely recommended, but it appears to me more likely to increase than diminish the hæmorrhage, unless, indeed, the bleeding ulcer happens to be in a coil of intestine which lies superficially, just beneath the abdominal wall. In very profuse bleedings we may have to face the question of stimulation. Half-teaspoonful doses of brandy given frequently by the mouth, the greatest care being taken not to improve the pulse too much, will often do all that is required. Or a small dose of saline solution, not more than 10 ounces, may be injected under the skin, and repeated when necessary.

When a diagnosis of *perforation* is made, the patient, if not absolutely moribund, should be operated on at once. In some hospitals time is saved by obtaining leave to operate, should necessity arise, from the relatives of the patient at the time of his admission, and there is much to be said for such a routine procedure. I have seen no accidents occur with chloroform or A.C.E. mixture in operable cases, but some surgeons prefer a local anæsthetic. From a study, at a large number of autopsies, of the situation of the perforation in the abdominal cavity, I believe that incision in the middle line below the umbilicus gives the operator the best chance of reaching the perforation, but, when symptoms point especially to the right iliac fossa, an incision in the right linea semilunaris is preferable. The ileo-cæcal valve should be located and the ileum examined. Should no perforation be found, attention must be directed to the large intestine. The greatest care must be taken in handling the bowel, which in enteric fever will not stand the same pulling about as, for instance, in appendicitis. Once the perforation is discovered it should be inverted, and sewed up with Lembert's sutures, or in very bad cases a continuous silk suture may be used to save time. Should there be little sign of peritonitis, it will be sufficient to wipe the coils of gut in the neighbourhood of the perforation. If, on the other hand, peritonitis is general, it will be necessary to flush out the abdominal cavity with warm saline solution. The stitched perforation should be brought as near as possible to the wound, and a gauze drain should be inserted, unless the condition of the peritoneum appears to be very satisfactory, in which case it can be dispensed with.

It must be recollected that sometimes peritonitis exists without perforation, and that occasionally the perforative symptoms are caused by a ruptured gall-bladder or mesenteric gland. If, in addition to the actual perforation, others appear to be threatening, it is wise to treat them as if the accident had already occurred.

Should operation be deemed impossible, all that can be done is to administer opium freely and give little or nothing in the way of nourishment, with the object of allowing adhesions to shut off the perforation.

It is highly undesirable to interfere with the course of the *temperature* unless hyperpyretic levels are reached, or prolonged temperature with little or no remission appears to be affecting the patient deleteriously. The frequent tepid or cold sponges, which should be used every four hours in severe cases, are usually quite sufficient. I have never seen any advantage, and I have observed instances of dangerous collapse, follow the use of the coal-tar antipyretics. And yet, so far as my experience goes, I should say that in general practice these drugs are still far too commonly used. They certainly lower the temperature, sometimes indeed too much, but they are apt to prolong the fever, and, unlike the cold bath, they seem to inhibit, rather than increase, the excretion of toxin in the urine. In cases of actual hyperpyrexia, of which I have seen very few examples, rubbing the patient with blocks of ice, the ice coil to the head, the ice cradle, the cold pack, or liberal sponging with ice-cold water are, as a rule, sufficient.

As regards the *nervous symptoms*, the early headache of typhoid may be treated with caffeine in 5-grain doses, or simple vinegar cloths may be applied to the head. Insomnia is often a troublesome condition. If, as is not infrequently the case, this depends upon worry, the patient not sleeping because he is anxious about losing his work and similar causes, I know nothing better than Dover's powder, as recommended by Foord Caiger. Before, however, any drug is given, various means may be employed by the nurse. The first of these is sponging with either tepid or cold water, which, by lowering the temperature about a degree, induces a sensation of comfort and assists the patient to fall asleep. Next a hot drink, either milk, or beef-tea, or even toddy, if alcohol is not specially contra-indicated, should be tried. If these fail various drugs may be employed. I prefer chloral, in the form of Liebricht's syrup, together with sodium or ammonium bromide, 20 grains of each, a half-dose to be repeated twice, at half-hourly intervals, if the patient is not asleep. This is usually successful before the whole 40 grains have been taken, though in rare instances another 10 grains of each may be required. The great thing is, having once started, to repeat till the patient is asleep. Chloral should not be given in cyanotic cases. Veronal, chloralamid, and paraldehyde are all useful on occasion. It is wise not to wait too long to see if a delirious patient will sleep. Each sleepless night will make his condition more intractable. On the other hand, one good night's rest often prevents the necessity of further drugging. Subsultus suggests that the patient is not

getting sufficient sleep and will often be much diminished by the judicious employment of a hypnotic. Retention of urine must be treated with the catheter and, should any cystitis be present, urotropin should be given systematically.

In cases of thrombosis the limb should be elevated and bandaged from the foot upwards. If there is much pain from phlebitis the parts may be covered with lint smeared with belladonna ointment. The other complications of convalescence may be treated on ordinary lines.

Stimulation. It is entirely a mistake to suppose that typhoid patients require alcohol necessarily as a routine. On the contrary, it is certain that much harm may be done by its indiscriminate use. The too liberal employment of stimulants in this fever is associated in my mind with such conditions as restlessness of the patient, irritability of the bowels, and increased liability to hæmorrhage. Of my own patients not more than one in ten is systematically dosed with alcohol. A slightly larger number get occasional single doses should necessity arise.

As regards the indications for stimulation, patients who are alcoholic will probably require it. Elderly patients, again, are much more likely to benefit from its use than are children and young adults. When the pulse becomes rapid, exceeding 120 in a male adult, when the first sound of the heart is almost inaudible, and when the tongue, in spite of appropriate treatment, remains very dry, the advisability of prescribing stimulants must be seriously considered. In cases, also, where there is marked pulmonary congestion, alcohol is often of great advantage. Even in these circumstances, however, its systematic and regular use may not be necessary, and often very small amounts, once or twice repeated, have all the effect desired. In every case the result of the dose of alcohol must be carefully noted, and if it does not favourably affect the character and rate of the pulse there is little use in persisting with it.

Alcohol may be found useful in small doses on certain special occasions. If the cold bath treatment is being systematically used, a small dose is prescribed by most authorities immediately after the patient is removed from the bath. Again, after irrigation of the large intestine, a prolonged and somewhat exhausting operation, it may be occasionally necessary to give a small quantity of spirits. Under certain circumstances, again, a little whisky, in the form of hot toddy, may be found useful as a soporific, if a cupful of hot beef-tea has failed, and if a hypnotic drug is not thought necessary. Even very small amounts have a sedative effect on nervous patients.

As regards the choice of stimulants employed, during the acute stage

there is probably nothing better than good Scotch whisky. This may be started in doses of even such small amounts as one drachm every four hours, and should rarely be increased beyond half an ounce at similar intervals. If there is much diarrhœa, or any tendency to sickness, brandy is more useful and is likely to be better tolerated. In convalescence many patients are much the better for a glass of port wine with their dinner and at night, and in private practice a good Burgundy may be employed at this time with great advantage. Stout is also an excellent form of stimulant to use in the convalescent period.

Drugs such as digitalis and strophanthus are most disappointing. Strychnine may be given with advantage, if no diarrhœa or restlessness are present. Goodall speaks favourably of spirits of camphor, 5 to 15 minims in port wine.

It may be said in conclusion that alcohol stimulation may often be postponed if strong beef-tea is used judiciously as a stimulant.

SYSTEMS OF TREATMENT. We have already seen that some of the dietetic systems mentioned above, in conjunction with appropriate interference should complications arise, may be regarded in themselves as systems of treatment. But special treatments, on antiseptic lines, with systematic cold bathing, and with various serums and vaccines, have also been much used, and are well worthy of a brief consideration.

Antisepsis. We may attempt to secure antisepsis by a variety of methods, the most obvious of which is the administration of antiseptic drugs. But apart from this we can try and keep the bowel clean, either by employing a diet which leaves little or no residuum, as described on a previous page, or by the combined use of aperient drugs and copious enemata.

We no longer believe with those who first introduced antiseptic drugs in the treatment of enteric fever, that we can attack successfully the bacillus in the intestine, or that we can counteract its toxins in the blood. But we may reasonably expect to secure a considerable antiseptic action on the contents of the bowel, and to delay and check putrefactive processes which, uninterfered with, might lead to the production of gas and the subsequent development of meteorism. It is possible also that a suitable general antiseptic might check the multiplication of the typhoid bacillus in the blood itself, if, indeed, any growth takes place there. For any real specific action we must, of course, wait for an effective antitoxic serum.

We know that many typhoid patients escape ulceration altogether. It is surely much more likely to occur in the presence of putrefying and fermenting matter than in a bowel in which these processes are reduced to a minimum, either by the use of drugs or some other method. The idea of antisepsis is

a clean one, and has much to commend it. But, putting the question of ulceration aside, it has always appeared to me that the pyrexia of an enteric fever patient often depends on two factors, the first toxic, with which at present, for the want of a suitable serum, we are unfortunately unable to deal; and the second, the septic factor, which, if not attended to, causes a superadded pyrexia by absorption of septic material from the gut. I find that the great majority of my patients average a degree to a degree and a half of temperature lower within forty-eight hours of admission. And this improvement, while partly due to proper diet and good nursing, is, in my opinion, chiefly the result of the attention which the bowel receives during the first two days the patient is in hospital.

About twenty-five years ago I made an extensive trial of intestinal antiseptics, and among other drugs used naphthol, salol, perchloride of mercury, calomel, guaiacol, and thymol. Of these, the most useful is naphthol β , which may be given in 6-grain doses every four hours. Salol is theoretically an ideal drug, as it is not decomposed into its antiseptic constituents till it reaches the lower part of the ileum. But its effect was much inferior to both naphthol and guaiacol, and it is more toxic than either when given over a long period. Perchloride of mercury is very effective, especially in reducing meteorism, but cannot be given long without fear of salivation. Of calomel I shall have something to say later. Of other remedies recommended we may mention particularly cinnamon oil, as suggested by Carne Ross, in 3 to 5-minim doses. It is important that only the best oil should be used. Foord Caiger has had satisfactory results with this drug, and also recommends sulphurous acid, 20 to 30 minims, as introduced by Wilks many years ago. Carbolic acid, in 1 to 3-minim doses, also has its supporters, as has Burney Yeo's mixture of chlorine water and quinine. The latter I have used extensively, and do not consider it as effective as many of the others. Ewart, in conjunction with his special diet, prescribes powdered charcoal and paraffin oil. I have used the former of these with but little effect.

Antiseptic drugs must not be expected to work miracles. They do not, in my experience, shorten the duration of the fever, nor do they prevent relapses. But, when given judiciously, they do not injure the patient, and they modify favourably the offensiveness of the stools. The tendency to meteorism, moreover, is much less when they are used. The effect on ulceration is disappointing. Hæmorrhage occurred among my patients in about the usual percentage of cases. I recommend the use of antiseptics, especially if a liberal mixed diet is being used, and it is often convenient for the general practitioner to prescribe drugs, if only as a placebo.

Antisepsis by elimination. For want of a better name I may describe,

under this heading, the particular treatment which I personally employ and have now used for many years. It consists in the use of aperient doses of calomel every second or third day, supplemented by irrigations of the large intestine with hot water. The patient is also encouraged to take large amounts of water to drink. The diet is that which I have described earlier in this chapter.

The use of calomel in enteric fever has been approved by many observers, from Liebermeister downwards. Its traditional employment has been to empty the bowel in the early days of the fever, and when the patient first comes under observation. It is said that, used later in the illness, it is apt to cause diarrhoea and colic, but this is certainly not the case if the large intestine is washed out with hot water at the right moment. So far as I can judge, calomel, in doses of 3 grains, empties the small intestine into the large. If the large intestine is not irrigated, or an enema is not given, a motion cannot always be counted on. The time to give this irrigation is not later than seven hours after the dose has been taken. The object with which the calomel is prescribed, in what might be called purgative doses, is to prevent any stagnation of fermenting material in the ileum. The drug has also a considerable antiseptic action on its own account, and it has been proved to limit the multiplication of the organisms of putrefaction in the gut. The objectionable matter having been removed from the ileum, it is not allowed to remain and irritate the large intestine, but is at once washed out.

In a series of 958 cases treated in this manner, my experience has been that the alleged dangers and disadvantages of calomel have not been noticed. As regards pain, the evidence of the nurses in charge, and my own observation, lead me to believe that it is seldom or never complained of. As regards diarrhoea, if it exists on the patient's admission, it quickly disappears under the influence of a suitable diet, and of the washing out of the large intestine. I have never seen it actually set up by the use of the drug. So far as perforation is concerned, the incidence in this series of cases was under 2 per cent. Hæmorrhage, however, occurred in over 8 per cent. of the cases, which is no less, though not more, than our usual average. We are justified in concluding that calomel does not increase the liability to ulcerative accidents.

The calomel is usually given in the early hours of the morning, at any opportunity which occurs without disturbing the patient, between 3 and 5 a.m. I find that all the effect desired can be obtained with a 3-grain dose, though doses of 5 grains can be given to adults with perfect safety. Children tolerate the drug well, and the ordinary dose, 3 grains, can be given to all who are not below three years of age, for whom a slightly smaller amount is

preferable. I have never seen salivation follow this treatment even when the calomel is given every second day for a fortnight or more, the dose being sufficiently purgative to eliminate itself. As defervescence sets in the drug is given less frequently, every third or fourth day, and, in convalescence, I prefer to move the bowel with 1 to 1½-drachm doses of castor oil.

To obtain the full effect, and to prevent colic or pain, an enema or irrigation must always be administered six or seven hours after the dose. Our attention was first drawn to irrigation of the large intestine by the papers of Buchman and Shuell. The former of these, however, used cold water with a view of controlling the temperature, a method which, in my hands, was responsible for more than one dangerous collapse. Seibert, also, and other supporters of a milk-free diet, have had admirable results from washing out the large intestine in this manner. Our method of *irrigation* is to allow 3 to 5 pints of hot water to slowly enter the bowel from a douche-can, raised only slightly above the level of the patient. The water is previously boiled, and is at a temperature of 116° to 120° F. in the can ; but as the process is a slow one, and there is a long stretch of rubber tubing, it is several degrees lower when it enters the bowel. If there is much diarrhœa, a teaspoonful of common salt to each pint may be added. The patient lies with the hips raised, and on the left side. A change to the right side, after a couple of pints or so have entered, often allows the amount of water introduced to be more readily tolerated. The largest amount I remember giving was 6 pints ; a very average irrigation would be from 3 to 4. A red rubber catheter attached to the tubing of the can allows the water to be discharged in the neighbourhood of the sigmoid flexure. The patient is directed to retain the fluid for as long as he can, and then usually passes not more than two-thirds of it. Sometimes a second motion is passed later. Much of the fluid is returned by the kidneys. The increase of diuresis is, indeed, in toxic cases one of the advantages of this form of treatment. The patients usually experience a great sensation of comfort after their irrigations, and not infrequently they demand more than are prescribed. In cases of meteorism or excessive diarrhœa two or three may be given in the twenty-four hours. As a rule, however, one, after each dose of calomel, is all that is required.

As regards contra-indications to the use of this treatment by calomel and irrigation it may be mentioned that, if meteorism is excessive, it is well to withhold the calomel and to be content at first with an ordinary enema or very small irrigation. It is wiser, indeed, to commence the treatment this way in any case, and to take an opportunity of inspecting the stool before giving calomel. If blood is present, it would be most foolish to disturb

a bowel which obviously requires perfect rest. Meteorism is sometimes temporarily increased after the dose of calomel, and before the irrigation. When the latter has been given, the distension is, as a rule, much reduced. In cases where the temperature is running along in a straight line with little or no remission, and where ulcerative accidents are expected, it is well to be cautious. Probably a third of the hæmorrhage cases in my series never received calomel at all, for this reason, and the same applies to the perforations. Only twice have I seen hæmorrhage occur on the day on which calomel has been given. In one case the first show of blood was in the returned water of the irrigation, and preceded a smart hæmorrhage.

TABLE C
RECORD OF 1,356 CONSECUTIVE CASES OF ENTERIC FEVER

<i>Number treated.</i>	<i>Treatment.</i>	<i>Percentage of</i>			
		<i>Deaths.</i>	<i>Hæmorrhage.</i>	<i>Perforation.</i>	<i>Relapse.</i>
397	Expectant	11·83	8·06	3·27	5·79
959	Calomel and Irrigation	8·86	8·02	1·77	4·79

The above figures show the results of this treatment. The list shows all admissions to hospital, and no deduction of cases fatal within forty-eight hours is made. It will be noticed that ulcerative complications are not more frequent in the group in which calomel was employed.

Value of large quantities of water. In addition to the medicinal treatment outlined above, I am accustomed to insist on the patient taking large quantities of water by the mouth. The forced ingestion of cold water, indeed, may be said to rank as a method of treatment by itself. About twenty-four years ago Débove succeeded in forcing 10 to 12 pints of water daily on his patients, and his results were extremely good. More recently, Cushing and Clarke have given 4 ounces of water to their patients every fifteen minutes during the waking hours, and in this way amounts varying from 8 to 14 pints were comparatively easily taken. Besides this, the patients had at least 3 pints of additional fluid, in the form of milk and albumin water, during the course of the day. The effect of such a treatment is very marked diuresis, and by this method it is hoped that the excretion of toxins is considerably increased. While I have seldom persuaded patients to take more than 8 or 9 pints of water, in addition to their fluid diet, I have noticed a very marked diminution and improvement of such symptoms as headache,

restlessness, delirium, and other toxic manifestations, and such results certainly point to a clearing out of the toxins from the blood. It was found by Cushing and Clarke that their cases, which were being treated systematically on the usual hydrotherapeutic lines, required the cold bath much less frequently, and, when we remember that the chief merit of cold bathing is the increased diuresis which it secures, such a result was only to be expected. The only disadvantage they noticed was that meteorism appeared a little more frequently than usual. Otherwise complications were rare. I have not noticed this tendency to abdominal distension in my own cases, but the amount of water which I have given has been, on the whole, less than that prescribed by the American physicians. The polyuria is said to counteract the retention of chlorides usually noticed in enteric fever.

It would be interesting to know if there is any risk of protective substances in the blood being eliminated, together with the toxins, under this method of treatment. Such an objection is probably only theoretical, for, as we have seen, the improvement of the toxic symptoms is such as to make us doubt that the resistance of the patient can be in any way weakened. It has been suggested, however, that the employment of saline beverages would tend to compensate any exhaustion of salts from the blood, and Todd prescribes 10 grains of sodium chloride with 5 grains of potassium bicarbonate in 8 ounces of water flavoured with lemon juice.

It is not very difficult to ensure patients receiving 6 pints of water in the twenty-four hours, in addition to their milk and beef-tea, and for some years I have endeavoured to lay this down as the minimum in our wards. Many patients will take much more, but, when there is much delirium, it is not always possible to give a larger amount than 6 pints. The increased diuresis is of the greatest value to the patient, and the elimination of more fluid by both lungs and skin helps to moderate the temperature. The method, either employed alone or in conjunction with some systematic treatment, possesses much of the advantage of the cold bath, especially if care is taken to keep the skin in condition by frequent cold spongings, and at the same time the labour entailed by systematic cold bathing is dispensed with.

Treatment by the cold bath. Although the use of cold water in the treatment of fever had been introduced in the closing years of the eighteenth century by Currie, its systematic employment in enteric fever dates from 1861, when Brand, of Stettin, devised the method which is so largely in vogue on the Continent and in America at the present day.

The technique of the method, as carried out strictly, is as follows. Whenever the temperature, taken in the rectum, reaches 102.2° F., the patient is placed in a bath at 65° . A compress, soaked in water at about 5° lower,

is placed on the head, or water may be poured over the head and shoulders. Compresses, dipped in ice-cold water, are laid on the chest and abdomen. The patient remains in the bath fifteen minutes, during which he is encouraged to rub himself, and is systematically rubbed down by the attendants. This is done to stimulate the peripheral circulation. About eight or ten minutes after the commencement of the bath, shivering usually begins, but this is to be disregarded, and the full time prescribed should be occupied in the process. The patient is then removed from the bath, and wrapped in a coarse linen sheet, over which a blanket is folded, the extremities being thoroughly dried and rubbed. A little alcoholic stimulant is then given. The bath is repeated every three hours, unless the temperature remains below 102.2° . No drugs are employed. The bath should be given at the bedside of the patient, who is thus disturbed as little as possible.

A first bath may be given at a slightly higher temperature, that of the room for instance. Neither age, sex, menstruation, pregnancy, constipation, nor diarrhoea are to be regarded as contra-indications. Young children are said to be particularly favourable subjects for this treatment. Hæmorrhage, peritonitis, phlebitis, and great prostration are, according to Osler, the chief conditions which demand the cessation of the treatment.

The advantages of the method appear to chiefly depend upon the greatly increased diuresis, and consequent elimination of toxins, and upon the general tonic effect. Gay suggests that the rigor and accompanying leucocytosis may also play some part. The pyrexia is usually temporarily reduced, but in some instances is almost unaffected. The treatment in fact is much more than an antipyretic one, and it does not appear that its supporters lay much stress on any reduction of temperature which it may secure. The pulse improves in rate and tone, the bronchitis is improved, and the risk of hypostatic congestion is said to be less. The frequent cleansing of the skin is of advantage in preventing bed-sores. The duration of the fever is unaffected, and it is not probable that the incidence of relapses is in any way altered. The death-rate has been much reduced in all hospitals in which the system has been thoroughly carried out, and, as the ulceration is unaffected, women benefit, on the whole, more than men. It is in toxic cases, particularly, that good results are to be expected.

The treatment has been much modified since the time of Brand, the general tendency being to make it less severe. Thus Osler prescribes his baths at 70° F., and does not hesitate to raise the temperature to 80° if the tubbing is not well borne. Goodall gives the bath every four hours, irrespective of the patient's temperature, at 80° to 85° F. At these levels the effect on the kidneys must be much less than when the treatment is carried

out on its original lines, but the results appear to be admirable. The strict Brand system has never obtained a real foothold in Great Britain, the cold bath being usually reserved for severe cases with much toxæmia and persistent high temperature. In its modified form, however, it is used in some hospitals. The labour which it entails is a serious bar to its general employment, and it is quite unsuited to private practice. In emergency, however, a very fair bath can be built up in a patient's bed with macintosh sheeting, and the patient satisfactorily drenched with cold water.

In my own view, if we remember that the tonic and diuretic actions of the bath give it its chief value, we can, by the frequent use of cold sponges or packs, on the one hand, and the plentiful internal administration of cold water on the other, sufficiently secure these advantages for our patients.

Treatment with colloidal metals. The use of these metals has been common in France for various infective conditions since 1902, when Netter drew attention to their value. Electrargol, collargol, and colloidal gold have all been given by intravenous injection. A violent reaction usually follows, accompanied by rigors, vomiting, cyanosis, and dyspnoea, after which the temperature rises to very high levels and may itself become a source of danger. Profuse sweating and a fall of temperature should then occur, and sometimes the pyrexia ceases altogether, although usually two or three injections are required. The symptoms thus resemble those we observe in protein shock therapy, and no doubt a leucocytosis has much to do with the resulting improvement. Salomon, who considers the shock symptoms too severe to be safe, speaks favourably of intramuscular injections of colloidal gold, and claims that he can obtain sufficient improvement by this means. Jouve-Balmelle also prefers intramuscular injection and gives 2 c.c. of electrauroil daily until improvement occurs. I hope to make a trial of this method, which appears to be safe and reasonably successful.

Serum Treatment. Enteric fever is not a disease which lends itself so readily as some others to serum treatment. The patients, as a rule, come comparatively late under observation, and the illness has thoroughly developed before a certain diagnosis can be made. Judging, then, from our experience of antitoxin in diphtheria, it is difficult to see how any results, at all comparable to those obtained in that infection, can be reasonably expected. Attempts have been made, however, to prepare a suitable serum, and from time to time these preparations have been put on the market.

The chief difficulty in preparing a typhoid antitoxin is the fact that the toxin of the bacillus typhosus appears to be an endotoxin, and its isolation is therefore hard to obtain. The first serums which were recommended for use were bactericidal rather than antitoxic in nature, and were produced

by the injection of typhoid bacilli into horses. Their bactericidal action was of little value, and I have seen no patient improved by their employment. Jez, recognizing this, attempted to prepare an antitoxin from the bone marrow, spleen pulp, and nervous tissue of immunized rabbits, Wassermann having found that these tissues contained protective substances. The extract thus produced was said to be antitoxic, but not bacteriolytic or agglutinative, and was given in relatively large quantities by the mouth. Unfortunately, my own experience of a dozen sharp cases of the fever, treated with this preparation, led me to discard it as useless, though it is said to have given good results elsewhere.

The most successful serum yet produced appears to be that prepared by Chantemesse, who claimed to have procured a typhoid toxin with which to immunize the horses employed. His results were admirable, only 4 per cent. of 765 cases, treated with his antitoxin, having died, while in the other Paris hospitals over the same period the mortality varied from 12 to 18 per cent. The serum is injected into the forearm in a dose of from 10 to 20 c.c., and is usually followed by a reaction. The pyrexia, however, quickly subsides. When a second dose is given, it is usually smaller, and the regulations for dosage read more as if it was a vaccine and not an antitoxin that was in question. The preparation has never been put on the market, and I have failed to find any confirmatory reports regarding it in the literature.

Very few reports as to the use of the anti-endotoxins prepared by Besredka and by Hewlett are available, and it would not appear that they have been really successful. There is more information regarding the serum of Rodet, who immunized horses with living typhoid cultures and also endotoxins. Several observers have reported favourably, and Martin considers that, if it is used before the eleventh day of disease, good results can be secured. But in the meantime we have still to wait for a reliable serum to be put upon the market.

Vaccine Treatment. While enteric fever would appear to be a disease in every way suited to vaccine treatment, and while many workers have given encouraging reports of their efforts in this direction, it is difficult at present to speak with any certainty as to the value of vaccines. We still urgently require records of long series of cases, properly controlled, before a definite pronouncement on the question is justified. My own experience has been small, and limited to a brief series of cases treated with doses much smaller than those now recommended. While the course of the pyrexia was in some instances profoundly modified, I was not satisfied that the treatment was particularly effective, and my experiments were brought to a conclusion by the commencement of the war, and want of time and assistance to do

anything more than routine work. I have, therefore, to depend upon the literature of the subject, which, generally speaking, is not very convincing.

Many varieties of vaccines are employed. They may be stock cultures or autogenous, prepared from the patient's own bacilli. The advantage of the latter is not necessarily very great; a stock culture, of a strain which has a proved capability of stimulating the production of antibodies, may be actually more effective. The cultures may be sensitized, or not; they may be living, killed by heat, or autolysed by ether. Lastly, they may be injected subcutaneously or intravenously.

The question of *dosage* presents obvious difficulties. Sadler was satisfied with his results and gave only 2,000,000 bacilli at an injection. This he usually decreased by half for a second dose. The late Professor Chantemesse, who kindly sent me some vaccine, recommended a dose of 60,000,000 organisms, to be followed, at five-day intervals, by 30,000,000 and then 15,000,000. Leishman has suggested an initial dose of 200,000,000 rising to 500,000,000, and Krumbhaar and Richardson recommend 500,000,000 for the first dose for an average adult, to be followed, if necessary, by two or three larger doses. Meakins and Foster used 1,000,000,000 as a first injection, 1,500,000,000 as a second, and 2,000,000,000 as a third. Other workers have given doses within these extreme limits, and the interesting thing is that most of them are convinced of the efficacy of the vaccines. The great discrepancy in the amounts injected raises a considerable difficulty. So far as can be judged, however, the high doses are safe and the results recorded of them probably more satisfactory.

There is, perhaps, less difference of opinion regarding the *interval* between the injections; while some have recommended daily doses, one of from two to five days is that favoured by most of the authorities. Wiltshire and MacGillicuddy think that shorter intervals than three days are not well tolerated, and that the longer the interval the more susceptible the patient is to the next dose. If the interval, then, is four days the dose should not be increased; if it exceeds four days the dose should be reduced.

The *subcutaneous injection* of vaccine may be followed by slight local reaction and occasionally some exacerbation of the temperature. But, generally speaking, reactions do not appear to be alarming, and, if the doses are not excessive, need not be feared. The majority of the observers appear convinced that the treatment is a useful one, and that both deaths and relapses occur less frequently. Perhaps the most convincing critic of stock vaccines used in this way is Whittington, who treated 115 cases with vaccines and a similar number by ordinary methods. The latter series gave better results as regards the mortality, the percentage of relapses, the duration of

the fever, and the occurrence of ulcerative complications. Whittington, indeed, believes that hæmorrhage is rendered distinctly more frequent, possibly as the result of a reaction in the Peyer's patches. He found also that patients with broncho-pneumonic complications did not do well with vaccines, a point already remarked on by Wiltshire and MacGillicuddy, who are enthusiastic believers in vaccine therapy.

On the whole I cannot believe that the supporters of this form of treatment have proved their case, but two modifications of the method, comparatively recently introduced, compel further consideration of the subject. The first of these is the employment of *sensitized vaccines*, and the second the adoption of *intravenous administration*. Gay has collected cases which seem to show that sensitized vaccines give, even when used subcutaneously, very much better results than untreated vaccines, and that when the results of intravenous injection are compared, the difference in favour of the sensitized vaccines, while not so striking, is still very considerable. It will be sufficient, then, to consider the intravenous administration of sensitized vaccines.

The injection into the vein of 150,000,000 of bacteria, or, as recommended by Gay, of one-fiftieth of a milligramme of sensitized vaccine sediment, is followed in about fifteen minutes by a rigor and a rise of temperature, from one to three degrees, which reaches its height in about three hours. This rise is accompanied by a leucopenia, and there may be slight cyanosis, dyspnœa, and a rapid pulse. The temperature then falls, with sweating, and becomes normal or subnormal in about twelve hours. With the fall there is a leucocytosis, sometimes up to 40,000, and a relative increase in polymorphonuclears. The special vaccine used by Gay, possibly owing to the fact that its endotoxins were removed, did not cause reactions which were in any way harmful, but other preparations appear not infrequently to give cause for real alarm. Gay has treated ninety-eight cases, of which thirty-three aborted and thirty-two were improved. The milder cases reacted better to the treatment. The mortality rate of the whole series was 6.6 per cent., a very satisfactory figure. Galambos employed the sensitized vaccine of Besredka in the treatment of 500 cases, and, after the first fifty, adopted the intravenous route, which he found in every way more satisfactory, except when heart failure is threatened or either hyperpyrexia or pneumonia is present. He used doses of 250,000,000 organisms, given daily on four to six occasions, and in 35 per cent. of his patients secured a crisis and early recovery. Relapses were rare, and the mortality was 9 per cent. Some of the reactions appear to have been fatal, and he now recommends doses of 125,000,000 to start with and not more than three injections.

The treatment thus appears to entail certain dangers, and further work

on the subject is much to be desired. A vaccine sediment as recommended by Gay would seem to afford most hope of success, and is probably without risk. We cannot read an account of the reaction without being struck by the fact that it is identical with that caused by the injection of colloidal gold, as mentioned in a former paragraph, and is due to the introduction of a foreign body, in this case a protein and also a colloid. Kraus has proved that the results are practically the same in 'typhoid' fever, whether the typhoid bacillus is the micro-organism in the vaccine or whether another germ, paratyphoid or colon, is employed, and this has been confirmed by other observers. Gay remarks that the results produced by typhoid vaccine cannot be regarded as specific in the narrower sense of the word. He attributes them to the leucocytosis which is set up, and to the co-operation of the patient's own antibodies acting as tropins and causing the digestion and destruction of the typhoid bacilli in the body by the increased white blood corpuscles.

There is much to be said in favour of the use of vaccines in the case of local inflammations, such as periostitis, following enteric fever.

PROPHYLAXIS. From the general public health point of view this will chiefly depend upon the supervision of the water-supply, the inspection of dairies, and the control of the collection and sale of shell-fish. Compulsory notification of actual cases is, of course, a necessity. In outbreaks recurring in a particular house or institution, for which no obvious cause exists, the possibility of a 'carrier' being responsible must be considered; and the urine and fæces of the inhabitants, particularly any who have had the fever at some previous date, should be examined for bacilli. In this connexion those persons who are concerned in the preparation and serving of food will first fall under suspicion. The drains must, of course, always be looked to, as, putting aside the possibility, doubtless remote, of infection through the medium of sewer gas, any leakage might, by contaminating the soil in the neighbourhood of a dwelling, cause infection by dust, or pollute water which, although not the regular supply for drinking, might occasionally be used for household purposes or for watering growing vegetables.

In widespread epidemics, especially before the cause has been definitely traced, the general public should be advised to boil their water and milk, or to drink aerated waters. In the latter connexion, however, it is well to remember that these waters themselves are not always entirely above suspicion. The food in the house should be kept covered from flies, which otherwise might play a considerable part in the dissemination of infection. Shell-fish should not be eaten raw when the disease is prevalent.

Isolation. When the fever has actually appeared in any house, the

patient should be isolated. If this is to be done successfully at home, a trained nurse, who appreciates the necessity of thoroughly disinfecting the excreta, is almost a necessity. The possibility of direct personal infection, especially in houses with small rooms and few conveniences, must never be forgotten. Flies should, as far as possible, be excluded from the sick-room, and the greatest precautions taken for the protection of the food of other persons in the house.

The custom of treating enteric fever in the ordinary medical wards of a general hospital is becoming less prevalent. It must, however, be admitted that when the proper precautions are taken, and when there is sufficient floor-space per bed, the risks are very small. Our custom at the City Hospital has always been to treat the numerous cases sent in for observation, or in mistake for enteric fever, in the same wards as the actual fever patients, and out of the many hundreds so dealt with in twenty-five years only one contracted the infection. Nevertheless it is probably advisable that all cases of enteric fever should be treated in an isolation hospital.

The *duties of the nurse* will be chiefly directed to the proper management of the urine and stools, both of which are highly infectious. She should take great care not to soil the bedclothes, or her own hands or dress, with either. The urine should be mixed with an equal bulk of 1-20 carbolic acid, and allowed to stand for at least half an hour, preferably longer, before being emptied down the drains. The stools should be similarly treated, a greater amount of the antiseptic being used, and it is safer to let them stand for several hours. The lid of the bed-pan should be left on, and the handle plugged with antiseptic tow. Most hospitals now possess arrangements whereby the excreta can be left standing in a cupboard, open to the air, but closed to the sanitary turret. Other antiseptics than carbolic can be used, the amount employed being regulated by the relative strength. I must confess, however, that I have always returned to carbolic, which, so far as I can judge, has given me the most satisfactory results.

The soiled sheets should be removed with care and without shaking, and the sooner they are damped with carbolic solution the better. To roll them up and place them in a bucket at the bedside is a good plan. They should then be wrung out of the antiseptic, and, the faecal stains having been brushed out, be finally left soaking in a carbolic tank (1-40) for six to twelve hours. This prevents any risk to the laundry attendants, who used in the old days to suffer so much. No laundry-maid, however, has taken the disease at the City Hospital in my recollection.

Nurses, on the other hand, as might be expected, are not so fortunate. It is night nurses, as a rule, who are most liable, and that no doubt for two

reasons. First, they seldom feel as well as they do when on day duty, and their digestion is often upset and their resistance no doubt proportionately impaired. Secondly, it is not always possible to make arrangements for them to have their midnight meal at a distance from the wards. It is highly desirable that they should always be scrupulously careful about washing their hands in antiseptics before eating, but when one remembers the ritual a surgeon goes through to procure sterile hands, far too long a process for any hard-worked nurse, we need not accuse them of uncleanness if they contract the disease. Some recommend that all food should be taken with a knife and fork. The use of rubber gloves, while the patient is being attended to, will obviously be a great protection to the nurse. Nowadays the prophylactic inoculation of nurses is becoming more generally practised, especially in America, and it is not unlikely that the Scottish Board of Health will soon insist on its practice in all fever hospitals. There is much to be said in favour of such an order, though I cannot help feeling that inoculation might lead to nurses being a little careless in technique, once the strongest of all motives, that of self-protection, is no longer active.

It is practically impossible in summer to exclude flies from wards with constantly open windows. The greater necessity exists, therefore, to see that the hospital dairy is fly-proof, and that the milk in all the wards is kept carefully covered.

Something can be done to limit the number of *carriers* allowed to be at large by systematic bacteriological examination of both stools and urine before a patient is allowed to leave hospital. Chronic carriers should, if possible, be kept under supervision and warned of the risks connected with their condition. The importance of careful washing of the hands after defæcation and micturition should be impressed upon them, and they should, if possible, be prevented from engaging in occupations concerned with the handling or preparation of food. It is advisable that their soiled linen should be boiled or otherwise disinfected before being sent to the laundry. Unfortunately there is no treatment at all efficacious for either the intestinal or the urinary carrier. Urotropine is stated to cause some diminution in the numbers of bacilli in the urine of the latter cases, and a combination of it with boric acid, called borovectin, is said to have effected some cures. Vaccines appear to have failed in both types of carriers, and intestinal carriers have remained equally unaffected by forms of treatment as simple as the administration of sour milk and as desperate as the extirpation or drainage of the gall-bladder.

Preventive inoculation. In 1897 Wright introduced the method of prophylactic vaccination with killed bacilli, and from the first obtained

gratifying results. Protective inoculation has been made practically compulsory in all armies, is advised for civilians proceeding to countries where the fever is endemic, and is being applied to secure the safety of nurses in many hospitals in this country and the United States.

As in the case of curative vaccines different methods are used to prepare the antigen, which may be killed by heat, be living, or be sensitized. The British vaccine is a culture attenuated at a low temperature, 53° C., and then finally killed with lysol; the American method is to use a slightly higher temperature, 55–56° C., and to add tri-cresol. The vaccines usually contain 1,000,000,000 bacteria per c.c. Vincent estimates that the minimum protective dose is between 1,300,000,000 and 2,000,000,000 bacilli, and states that the immunity and its duration are in direct relation to the number of micro-organisms injected and not to the number of injections. It is none the less customary to give at least two and sometimes three or four injections, and an interval of ten days is usually recommended.

The first year of the war showed that antityphoid inoculation was not sufficient, but that anti-paratyphoid protection was also required. Most armies, therefore, adopted a vaccine against not only the typhoid, but both paratyphoid organisms, the so-called *T.A.B. vaccine*. Dreyer and his co-workers have recommended a preparation containing 1,000,000,000 typhoid, and 750,000,000 of each of the paratyphoid bacilli to the c.c., and advise a dose of $\frac{1}{2}$ c.c., to be followed about eighteen or twenty days later by 1 c.c. as a second dose. This multiple vaccine seems to be tolerated as well as the simple one.

The vaccine should be injected subcutaneously either in the subclavicular or deltoid regions. It is contra-indicated in cases of severe organic disease, tuberculosis, arterio-sclerosis, diabetes, and renal insufficiency.

The reaction is seldom severe. There is some pain and swelling which rarely extends far from the site of injection, and the temperature may rise to 101° F., though in my own experience I have seldom seen it exceed 99°. There is some malaise and headache, but these symptoms do not as a rule last long. The reaction tends to be severe if the patient is fatigued or ill, and if such conditions exist it is wise to postpone inoculation. Allowance should also be made for at least twenty-four hours rest after the injection.

It seems probable that the *immunity* conferred by inoculation lasts, in the average individual, for about two years. Musehold, however, recommends re-vaccination every six months for troops, and Bruns also states that immunity cannot be depended on after that time. It was to test this immunity that Gay and Force introduced the typhoidin reaction (see p. 324). If this is negative a month after inoculation, a further course of vaccine should

be given. If positive, the test may be tried again after two years. The application of this means of testing immunity would seem to be advisable in countries where the risk of enteric fever is always present.

As regards the *value of inoculation* it may be said that the inoculated are very much less liable to take enteric fever and, if they do take it, probably have a relatively mild attack. All statistics appear to agree as to these particulars, which are confirmed by the experience of the British army in the war. During the first two years 1,501 cases of typhoid fever occurred, 993 among the inoculated, and 508 in the uninoculated. As fully 90 per cent. of the men serving had been inoculated, it would appear that the vaccinated were approximately five times as well protected as the unvaccinated. Some recent statistics, referring to 2,500 cases of enteric fever of all varieties, published by Webb Johnson, show that the mortality of 821 cases of typhoid fever in the inoculated was only 3·28 per cent., as against 19·19 per cent. in 297 uninoculated men, a similar, if not so marked, difference being noted in the paratyphoid fevers. Hæmorrhage occurred in 1·21 per cent. of the inoculated and in 13·46 of the uninoculated, while the figures for perforation were 0·36 and 2·02 respectively.

Repeated inoculations do not cause anaphylaxis, and there is, therefore, no objection to re-vaccination. The prejudice which at one time existed against inoculating during an epidemic for fear of infection during the negative phase appears to have been overcome, and some observers claim that the vaccination may act curatively if the patient is by any chance incubating the disease. In any case an almost immediate protection can be obtained by the use of sensitized vaccines, which, owing to the serum in which they have been treated, confer at once a short-lived passive immunity while the active immunity is developing. Gay also claims that the interval may be made very short, injections being given every second day, without any harm resulting, and such a procedure might be found very valuable in emergencies.

CHAPTER X

DIPHTHERIA

Etiology: predisposing causes, modes of infection, 'carriers,' &c.

Bacteriology: the bacillus and its toxins.

Pathology: the false membrane, the lungs, heart, kidneys, suprarenal glands, and nervous system.

Period of Incubation.

Clinical Features: symptoms of invasion, appearances in the throat, the glands, the temperature, pulse, appearance of patient, albuminuria, erythematous rashes.

Types of Faucial Diphtheria: mild types, moderate types, severe types, septic type, hæmorrhagic type.

Laryngeal Diphtheria: croup: tracheal diphtheria.

Nasal Diphtheria.

Diphtheria in other situations: vulva, prepuce, conjunctiva, buccal mucous membrane, skin, wounds.

The Heart and Circulation in Diphtheria: the pulse, heart failure.

Post-diphtheritic Paralysis.

The Blood in Diphtheria.

Complications.

Relapses and Second Attacks.

Diagnosis: general considerations, clinical diagnosis, differential diagnosis from various forms of sore throat, scarlatina, Vincent's angina. Diagnosis of laryngeal diphtheria.

Bacteriological Diagnosis: smears and cultures.

Prognosis.

Treatment: Serum Treatment: preparation of antitoxin, its value, its dosage, its administration, 'serum sickness', anaphylaxis, local treatment, general treatment, diet, treatment of heart failure, of paralysis, of laryngeal diphtheria, operative interference, intubation, tracheotomy.

Prophylaxis: isolation: management of carriers. Immunization by serum, by toxin-antitoxin mixtures: Schick immunity test.

Synonyms—French, *Diphthérie*; German, *Diphtherie*.

ETIOLOGY. Since the year 1883, when Klebs described the bacillus which we associate with the names of himself and Löffler, our knowledge of diphtheria has been constantly increasing, and to-day it is one of the few diseases for which there is a definite specific treatment. The discovery of antitoxin did much to stimulate the interest of the profession, and the therapeutic successes attained by its employment have led to an enormous amount of research, directed towards the application of similar methods of treatment in other infectious conditions. The bacillus itself has been made the object of much study, and to give any idea of the bacteriology of the subject, particularly as regards the micro-organisms which are termed 'pseudo-diphtheritic', would require a large volume. We must limit

ourselves here to a few elementary facts, such as are necessary for the practitioner to know.

Before, however, touching on the bacteriology of the disease it will be well to consider the conditions which favour its spread, and the modes in which its infection is disseminated. Its *geographical distribution* is general, though it is probably more frequently met with in the northern hemisphere than in the southern. As regards *season*, diphtheria is less common in the summer than in the winter months, and, in my experience, is most fatal from November to January. Damp cold weather increases the liability to the laryngeal variety of the disease, and this would to some extent explain the higher mortality often noticed in winter. According to Newsholme the disease is most prevalent in years in which the rainfall is deficient, and great epidemics usually follow a series of dry years. In wet years, on the other hand, the prevalence is less. The suggestion is that the bacillus is capable of leading a saprophytic existence in the soil. This is exceedingly probable, as unquestionably outbreaks of diphtheria occasionally follow the disturbance of earth by digging operations and the opening of long disused drains.

In the first ten years of life *sex* exercises little or no influence, but after the age of ten females show a greater apparent susceptibility than males. I say 'apparent' because, even at that early age, young girls are often employed in looking after their younger brothers and sisters, and are thus brought into more intimate contact with possibly infectious children than are males of the same age. In any case, from the age of ten onwards a greater number of females than males are affected by diphtheria. Another obvious cause for this is the feminine habit of indiscriminate kissing, which can hardly fail to increase the liability to an infection so readily communicated by direct contact, and so apt to lurk unsuspected in the throats of apparently healthy persons. Of more importance than sex, however, is the question of *age*. Diphtheria is essentially a disease of the first ten years of life, and especially of the first five years of life. Infants of under six months have in most instances an inherited immunity which can be demonstrated by the Schick test, but this wears off towards the end of the first year of life, and in the second year the disease is very common, occurring most frequently of all during the period from two to five years. It may be said broadly that the whole period from one to twelve years covers the vast majority of the cases which occur in this country, and it is interesting to note that these limits roughly correspond with the period of school attendance. The chances of infection, then, are naturally much greater at this time of life than at any other, and, were it not also the fact that the mortality is relatively highest in

the same period, it would not be necessary to assume that children are much more susceptible than adults.

Modes of infection. The infection is derived from a patient or a healthy carrier, and the simplest mode is by *direct contact*. The mother who persists, against advice, in kissing a child suffering from the disease, the practitioner who endeavours to clear a tracheotomy tube by sucking it, have too often illustrated how diphtheria may be contracted in this manner. Analogous to such direct modes is the transmission of the disease by a patient coughing or sneezing infected particles into the mouth, face, or eyes of an attendant or friend. Infection, however, by *indirect contact* is perhaps more common, and its possibilities may be best seen among school-children. The use in common of such articles as slate pencils, penholders, and the like, affords many opportunities for the spread of diphtheria, especially when we recollect how much the reflective sucking of the objects in question appears to aid study. Most of us, also, must have seen certain hard sweets, of the lasting variety which dissolve slowly, passed from mouth to mouth among children. The common use, again, of towels and even handkerchiefs in schools assists in the dissemination of infection. In any of these cases, indeed, all that is needed for the start of an epidemic is a child harbouring bacilli in the throat. It is easy to see how the various objects named can become infected, and the bacillus may remain active in fomites for a considerable time. Schools play a most important part in keeping alive epidemics of diphtheria, and, as we have said above, their influence is such as to have a marked effect on the age incidence of the disease.

Another method by which the bacillus can be conveyed to the human subject is by means of *milk*. Milk epidemics have been attributed to an ulcerated condition of the udders of cows, but as a rule it will be found that some one employed in the dairy is suffering from diphtheria. Only a cough or sneeze, or even merely breathing into the milk, would be quite sufficient to infect it. The bacillus grows well in milk without in any way altering its appearance. Our experience in Edinburgh has been that a dairy origin may be suspected for any outbreak which includes an undue proportion of adults. The vast majority of our patients being usually children, a large number of adults, who, as a rule, have fewer chances of contracting the disease by either direct or indirect contact, always suggests the necessity for most careful inquiry.

Outbreaks of diphtheria are often associated with bad sanitary conditions, and *defective drains* are frequently found in the houses of affected persons. But it is probable that life in a house with bad smells is more a predisposing

than an exciting cause, and that it merely favours diphtheria by causing relaxed and inflamed throats. In such throats, should other possibilities of infection be present, the bacillus easily finds a nidus. It cannot indeed be doubted that *catarrhal conditions of the throat* increase the predisposition to diphtheria, and the increased prevalence of the disease in the early winter is probably to a great extent the result of the action of the damp foggy weather upon the mucous membranes of the throat and larynx. Any condition which lowers the resistance of the mucous membrane increases the liability to the disease. The state of the fauces, for instance, after scarlatina, and of the larynx after measles, appears to offer a most favourable nidus. In the days, moreover, before the introduction of antitoxin, when strong antiseptics were in vogue as the best method of treatment, it was common to see the membrane spread rapidly in situations, previously healthy, which had been liberally swabbed, and it is reasonable to suppose that, if too strong preparations were in use, the tissues were sufficiently damaged to encourage the spread of the lesion.

It is probable that an actual breach in the mucous membrane, no doubt microscopic in size, is required before the bacillus can effect a lodgement. In a really healthy throat it is beyond doubt that virulent bacilli may be present for a long time without doing harm. Such throats may have received the micro-organism by the ordinary methods of direct or indirect contact, but, being in a healthy condition, diphtheria does not affect them. The bacillus, however, may live for months on the mucous membrane, and may be transmitted by direct or indirect contact to a person whose mucous membranes are not in a condition to resist inoculation. Convalescents, again, from diphtheria may harbour the bacillus in their throats for long periods. Such *carriers* are apparently a numerous class, and systematic bacteriological examination of school-children has often brought them to light in school or hospital, the bacillus being found to be present either in the throat or nose. They play a most important part in the causation of outbreaks of diphtheria.

As regards the part played by various *domestic animals* in disseminating diphtheria the best veterinary expert opinion appears very sceptical. Cats may possibly carry infection in the same way as it is carried by fomites, but the disease which has been called diphtheria in the cat has no relation to true diphtheria. It may be also asserted with some certainty that the so-called avian diphtheria, as observed in pigeons, is a quite distinct infection. Gofton, in an able review on Klein's experiments on cows, concludes that, while it is possible for the diphtheria bacillus to live as a saprophyte on already existing sores on the udder, cows do not suffer from diphtheritic infection.

BACTERIOLOGY. Diphtheria is due to the bacillus first described by Klebs in 1883, and successfully cultivated and further investigated by Löffler in the following year. The bacillus, named after these observers, is a slender rod, either straight or slightly curved, and usually about $3\ \mu$ in length. There are, however, long, short, and intermediate forms. It takes up basic aniline dyes readily and may be conveniently stained with methylene blue. Thus coloured, the appearance is occasionally uniform, but much more usually a dotted or beaded appearance is presented, owing to the presence of small granules which stain more darkly. The ends may be swollen or tapered. If looked for in diphtheritic membrane bacilli may be found either in clusters or irregularly scattered. They are not found in chains, but two may lie end to end and are apt thus arranged to present V shapes. Occasionally the membrane may show but few other micro-organisms, but, as a rule, streptococci or staphylococci are present in larger or smaller numbers, and sometimes greatly predominate, only a few scattered, bacilli being seen.

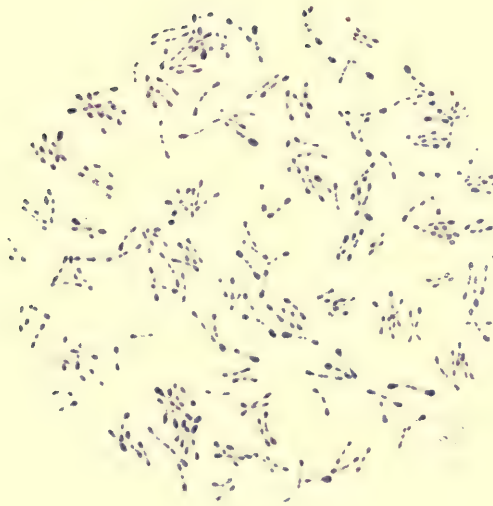
As regards cultivation, the bacillus grows well at the temperature of the body, the most favourable medium being solidified blood serum. Small circular colonies of a whitish colour appear often within twelve hours. The bacilli on culture are at first fairly uniform in size and shape, but stain more irregularly than when examined in a direct preparation. Involution forms appear in older cultures, and the rods differ much in shape and appearance, club-shaped and barred forms being met with. (See Bacteriological Diagnosis).

The bacilli can live for long periods in dry membrane, especially if they are kept in the dark. The presence of light or moisture, however, lowers their power of resistance, and they are, except in the dry state, readily killed by an exposure to 60°C . It is obvious, then, that very careful disinfection of articles, possibly contaminated by the micro-organisms of a patient, will be necessary if further outbreaks of the disease in the same house are to be prevented.

When cultivated in beef bouillon the bacilli give off *toxins*, as is proved by the fact that, if the fluid is cleared of the bacilli by filtration, the filtrate is capable, even in extremely small doses, of causing the death of small animals such as guinea-pigs and rabbits, paralytic symptoms appearing if death does not occur too rapidly. This filtrate, usually spoken of as diphtheria toxin, apparently contains a variety of poisonous substances, one of which is responsible for the local œdema which follows inoculation into animals, another for the acute symptoms of blood poisoning or toxæmia, and a third for the late effects on the nervous system as manifested by



A



B

A—HOFMANN'S BACILLUS. Twelve hours' blood serum culture.
Modified Neisser's stain. $\times 1000$.

B—KLEBS-LÖFFLER BACILLUS. Twelve hours' blood serum culture.
Modified Neisser's stain.

paralysis. Moreover, it has been proved that different bodies in the filtrate have a different degree of affinity for antitoxin, and that the substance which unites most freely with it possesses only a slight degree of toxicity. This substance has been termed 'prototoxoid', and until it is neutralized by antitoxin, the real toxin remains unchanged. Further addition of antitoxin, however, will neutralize the toxin, whereas another body, which has been termed 'toxone', is only capable of forming loose combinations, as it were, with molecules of antitoxin, after all the toxin present has been already taken up. It is the toxone which, it is believed, causes paralysis, and this explains to some extent the fact that paralysis is still a common sequela of diphtheria even when serum treatment has been employed, this particular poison having such a slight affinity for antitoxin that much of it often remains unneutralized.

PATHOLOGY. The bacillus, having effected a lodgement in some microscopic breach of the mucous membrane, causes locally the fibrinous exudation which is characteristic of the disease. There is degeneration, necrosis, and desquamation of the superficial epithelial cells, and the process continuing with much exudation of fibrin, the membrane is gradually formed, and increases in thickness. Microscopically the *false membrane* is found to consist of an interlaced network of fibrin containing red blood cells, degenerated epithelial cells, and here and there clumps of bacilli. The latter may occur all through the thickness of the membrane, but are often best seen in the lower and newer layers. There is in most cases some admixture of pyogenic cocci, and these, as might be expected, tend to lie more superficially. In addition to the local formation of the membrane, the bacilli are active in the production of toxic substances which are taken up by the lymphatics and the blood-stream. It was for some time held that the bacillus was only to be found locally, but its presence in different parts of the body proves that it also may be carried by lymph or blood from its original point of attack to other situations in which it may continue to give off toxins. The disease then, though originally local, may become, to all intents and purposes, general, though it is not to be doubted that the great poison factory is at the original site of inoculation. The superficial layers of the subjacent epithelial cells being practically destroyed, channels are opened up for the absorption of the toxins, and the more the local lesion spreads, and the more situations supplied liberally with lymphatics are affected, the greater is the resulting toxæmia. Besides the mere local extension of the false membrane the disease may be inoculated in new situations by the fingers of the patient, or by the inhalation of infective debris. The bacillus carried to a fresh site causes therein the same local changes as at the original point of inoculation.

A common site to be infected either by direct extension of the membrane downwards, or by inhalation, is the *lungs*. Formerly it was customary to regard the broncho-pneumonia, so commonly seen complicating laryngeal diphtheria, as a septic process. Especially was this the case if the condition occurred after tracheotomy. But bacteriology has proved that the bacillus is not only often found in the inflamed areas of the lung, but is not infrequently the only micro-organism present. That in many cases strepto- and pneumo-cocci play a great part in the causation of broncho-pneumonia there is, of course, no doubt, but occasionally their influence is unimportant, as is, I think, conclusively proved by the admirable results obtained by pushing antitoxin in the treatment of these lung inflammations. It may be added that Flexner has succeeded in experimentally producing pneumonia by inoculating the trachea of rabbits with diphtheria bacilli. The infection of the lungs is believed to occur through the bronchi, and not through the blood-stream.

The bacillus has been frequently found in the spleen, liver, kidney, heart's blood, and in abscesses in various situations. Its presence has also been noted in the lymphatic glands. Any changes, however, shown by these organs are attributed rather to the action of its toxins.

From a clinical point of view our interest is mainly centred in the effects of the toxæmia on the heart, the kidney, and the nervous system. The *heart* suffers severely from the first in a bad case of diphtheria, and the degeneration of its muscle is probably the earliest pathological change noticeable. In patients who have succumbed in the first three or four days of the illness the commencement of a fatty degeneration of the fibres has been demonstrated. Very minute fat granules may be the first sign. Later larger globules may be seen in the myocardium, and ultimately individual fibres may be completely destroyed. Hyaline masses are often found in place of the destroyed muscle elements, and the cells show vacuolation and may become fragmented. Although it has been suggested that these changes may be secondary to primary damage sustained by the cardiac nerves, there is every reason to believe that the degeneration is the result of the direct action of the toxin on the muscle itself. This toxic influence is, no doubt, responsible for some cases of the early progressive cardiac failure so frequently met with in the disease. On the other hand, it is probable that some cases of syncope occurring later, at a time when paralytic symptoms have appeared in other parts of the body, are due rather to the damage which the toxin has caused to the vagus.

The *kidneys* of fatal cases always show degenerative change. This may be limited to some cloudy swelling, and, occasionally, slight fatty

degeneration. In other cases there may be desquamation and destruction of the cells lining the tubules. Hyaline degeneration is said to be always present to a greater or less extent. Interstitial changes are not infrequently found, and, if well marked, the size of the kidney may be much increased. The interstitial tissue is infiltrated with lymphoid cells. The glomeruli suffer less frequently, but are sometimes found to be inflamed. Hæmorrhagic nephritis is rare. Bacteria may be found in the kidney, but the lesions are believed to be due to the toxin of diphtheria. The *suprarenal glands* may show degeneration, and hæmorrhages have been not infrequently observed in their substance.

Perhaps the most characteristic toxic lesion is the degeneration which affects the *nervous system*. This is observed in the peripheral nerves. The medullary sheath degenerates and is broken up into globules. The axis cylinders become involved and may be broken across. The primitive sheath remains intact. As a result of the rupture of the cylinders the nerve fibres below degenerate. Both sensory and motor fibres may be affected, but owing to some fibres remaining intact the paralysis caused is usually only partial. The work of most observers goes to prove that the condition is purely a peripheral one, but Rainy and others have described changes in cells in the anterior cornua of the spinal cord, and regard the nerve degeneration as secondary. The muscular fibres innervated by the damaged nerves may show extensive degeneration.

INCUBATION. This period is not always easy to determine. It is not difficult to fix the minimum limit, but when we come to the maximum we have to remember that the bacillus may exist for a long time in a healthy throat without infecting the person who carries it. It is quite conceivable, then, that after the infecting agent has reached the throat a considerable period may elapse before true infection occurs. A bacillus, which at first has found no opportunity of doing harm, may ultimately, through some microscopic breach in the mucous membrane, or from a lowering of the resistance by some simple throat inflammation, succeed in causing infection. It is possible to explain the occurrence of diphtheria in a measles or scarlatina convalescent on the assumption that he has harboured for some time micro-organisms, which have not previously had a fair chance of infecting him. The exact moment at which the infection occurs cannot be determined. And without a knowledge of the exact moment we cannot estimate the maximum limit of the incubation stage. On the other hand, there seems little doubt that the disease may develop within twenty-four hours of infection. Diphtheria has been contracted as the result of particles of exudation material being coughed directly into the mouth of a doctor or

attendant, and in those cases the latent stage has sometimes been extremely short. As an ordinary rule the disease appears to develop in two or three days after the exposure, and it is usual to assume that the longest incubation period does not exceed a week. The point is of little practical importance. For purposes of quarantine a knowledge of the maximum limit is no longer required, as it is customary to make bacteriological examinations of the throats of contacts.

CLINICAL FEATURES. Diphtheria is found in many situations, and as a result it is impossible under one heading to give a complete account of the course of the disease. It is most commonly, however, faucial, and it is this variety which it is convenient to regard as a type. The membrane may, of course, extend from the fauces to the pharynx or larynx, or upwards into the nasal cavities, or it may be limited to any one of these sites. It may also be found on the vulva, on the prepuce, on the conjunctiva, or on the surface of a wound or abrasion. Wherever situated, it causes in the majority of cases certain constitutional symptoms, and any differences between these varieties of diphtheria must be sought for in relation to the local results of the infection. These will be discussed later, when the peculiarities of each localization of the disease come under our consideration.

SYMPTOMS OF INVASION. The invasion period of diphtheria is extremely short. Fever is in the majority of instances the first symptom. There is a rise of temperature, seldom to high levels, 100° to 103° covering the usual variations (Fig. 46). Accompanying the pyrexia are the ordinary febrile symptoms of headache, malaise, chilliness, and indefinite pains. Most patients show considerable lassitude from the first. The pulse is apt to be rapid, 110 to 120 or even more, and is often soft. The appetite is lost and occasionally the patient vomits. Some degree of sore throat is early complained of by most patients who are able to do so. On the whole, severe prodromal symptoms are rare, but delicate children may suffer from rigors, or even convulsions.

The appearances in the throat. It is usual to describe a preliminary stage of catarrhal congestion as occurring in the locality where the membrane is going to form. Doubtless such *congestion* is a necessary stage in the development of the lesion, but in my experience spotting or patching is usually to be recognized practically as soon as it is looked for, which, among scarlatinal convalescents in a hospital for instance, is as early as a rise of temperature or other striking symptom is noticed. The symptoms of the commencement of the attack, then, may be regarded for all practical purposes as synchronous with the appearance of the lesion on the throat.

The first sign of membrane is usually the presence of one or more minute patches in the fauces. The commonest *situation* is unquestionably the tonsil. Sometimes both tonsils are affected from the first. The primary situation may, however, be the uvula or the pillars of the fauces, the posterior pillars in particular being a comparatively frequent site for the first appearance of the lesion. Much more rarely the local condition may be first noticed on the posterior pharyngeal wall. At this early stage the exudation hardly deserves the name of *false membrane*. It often wipes off comparatively easily, not yet having become intimately connected with the subjacent mucous membrane. It is merely a thin pellicle, soft in consistence, and fairly easily broken up. If removed, however, it very rapidly reappears, and when left alone soon becomes more firmly consistent and more securely attached to the underlying tissues. Its tendency is to spread rapidly over the surrounding structures.

Within twenty-four hours of the onset the lesion has probably assumed the characteristics of the diphtheritic membrane. When there is but little associated coccal infection the *colour* is usually greyish in colour. If thin, the membrane is translucent. The colour, however, varies considerably, its tints no doubt depending largely on the different micro-organisms which may be present. It is often pale yellow, sometimes dirty white, and occasionally a bluish or even greenish tinge may be noticed. In severe cases, where there is effusion of blood, the membrane may be dark and almost black in colour. It is usually firmly adherent to the subjacent mucous membrane. In the early days of the illness it can only be detached with difficulty and usually leaves a bleeding surface behind it. Thick membranes in particular leave a raw sloughy-looking surface which bleeds freely. Later in the disease, when the natural tendency for the membrane is to separate, it may often be detached without causing any hæmorrhage. It must, of course, be remembered that pultaceous soft exudations, which may be met with in some cases of diphtheritic infection, wipe off with comparative ease, leaving the mucous membrane which they covered only slightly modified in appearance, a pale greyish area being all that is to be observed. The separated membrane is, however, in most cases tough and consistent. It can be floated out in water and will stand considerable pulling about without tearing. It is sometimes quite leathery in its consistence.

When the membrane is spreading, it is surrounded by an area of deep congestion which shows itself as a narrow red margin round the edges of the lesion. This margin no doubt represents the congestive stage which precedes the formation of the actual membrane. It is often well seen on the palate and uvula. The *extent* of the membrane in the throat varies very

considerably even in untreated cases. It is, however, quite common for the process to spread from the tonsil and involve the anterior and posterior pillars, the soft palate and uvula, the opposite side of the fauces, and the posterior pharyngeal wall within a space of forty-eight hours. Occasionally the spread is even more rapid. On the other hand, the local lesion may limit itself from the first, and may only affect the tonsil on which it started.

It is well to remember that the membrane is not always continuous. There may be several simultaneous foci of infection, and the process may spread from each. Not infrequently the first manifestation of the disease on the tonsil gives quite a suggestion of follicular tonsillitis. The whole gland is covered with minute yellowish spots of exudation. In such a case the diphtheria appears to have originated in many of the crypts of the tonsil, and a pellicle spreads from each until it coalesces into one uniform membrane. In some outbreaks this type of onset seems to be much more common than in others.

The unaffected mucous membrane may show considerable congestion and oedema. This, however, especially when there is not much super-added infection, is much less than is usually noticeable in septic scarlatina. The soft palate particularly may be quite pale except at its extreme margin. The more pure the diphtheritic infection, the less is the redness and swelling of the throat, and consequently the less is the *pain* complained of. It cannot be too much insisted on (we shall have to refer to it again later) that diphtheria is in itself not a painful disease. The sore throat is often trivial even in bad cases, and children may swallow without difficulty even when there is membrane plastering all the fauces and pharynx. On the other hand, it is obvious that, if various associated organisms, which are septic in character, are present, both the pain and oedema may be well marked.

There is usually a distinctly unpleasant *odour* from a diphtheritic throat. In severe cases this may be exceedingly putrid. Some of us think that the smell is more or less characteristic, and that it is of assistance in distinguishing sloughy-looking throats, which depend on infection with the diphtheria bacillus, from merely septic ones.

In a case in which antitoxic serum has not been employed, one of two things may happen. Firstly, the natural tendency to cure may assert itself, and the spread of the membrane from its original situation may be extremely limited. In such a case the membrane may either separate *en masse* or may be gradually disintegrated and come away in shreds. In a very large proportion of serum-treated cases this disappearance of the membrane by a process of disintegration may be noticed. If, on the other hand, the spread of the membrane is not arrested, it may end by

involving all the mucous membrane in the mouth, if the infection is a particularly severe one. The hard palate, the buccal mucous membrane, the tongue, and even the lips, are sometimes attacked. The spread upwards of the lesion into the nasopharynx is evidenced by discharge from the nose, at first clear, after a short interval purulent. Extension downwards into the larynx and trachea is accompanied by such symptoms as aphonia, a croupy cough, and dyspnoea. From the trachea the membrane may spread into the finest ramifications of the bronchial tubes. But even in these severe cases the natural tendency of the membrane is ultimately to separate, and very often this separation may be completely effected before the patient succumbs.

The glands. Closely related to the lesions of the throat is the enlargement of the neighbouring glands, which is apparently due more to the toxins of the disease than to the bacillus itself. The glands most commonly affected are the submaxillary, those at the angle of the jaw, and the anterior cervical group. In slight cases the enlargement may be very trivial, and only some slight degree of tenderness be noted. Patients, however, who suffer from a severe throat condition may have a regular collar of matted and swollen glands all round the throat. When there is not much mixed infection the glands as a rule, however, remain distinguishable and there is no matting. Suppuration, again, which occasionally occurs, is only to be expected in cases in which septic organisms play a prominent part. The more pure the diphtheritic infection the less likely is suppuration to occur, even when the glands are intensely swollen and extremely hard. In septic cases there may be much sloughing of the infiltrated masses.

The temperature. We have already seen that some pyrexia usually accompanies the onset of the disease. It seldom, however, attains high levels, and often declines within two or three days. In a pure diphtheria, if it has any relation to the local condition of the throat at all, I would be tempted to say that the worse the lesion the lower the temperature. In septic cases it is more apt to remain moderately elevated for some days, but even here it would seem that the depressing effect of the diphtheria toxins does much to counteract the tendency of the septic infection to cause high temperature. No doubt the influence of antitoxic serum has done much to assist in reducing the fever, but the fact remains that, even in the pre-antitoxin period, cases quite commonly ran their whole course without pyrexia, and that these cases were often the worst. We may expect, however, even now to find moderate fever lasting from three to five days in the average case. The throat lesions quite frequently last

considerably longer than does the pyrexia (Figs. 46, 47). Fatal cases have often a subnormal temperature for some days before the end.

As regards the *pulse* it may best be considered in connexion with cardiac failure. During the early stage of the disease we have seen that it is apt to be somewhat more rapid than the pyrexia warrants. After one or two days it is more likely to bear a direct relation to the height of the

temperature. It is somewhat soft and compressible, and towards the end of the first week it may become unduly slow, particularly in adults.

The appearance of the patient.

The diphtheria patient is usually languid, and his appearance and expression suggest that he is so. The feeling of lassitude, so characteristic of the onset, often becomes more pronounced as the disease advances. The face in an averagely severe case is pale and the expression apathetic. In the worst cases the patient has a 'poisoned' look, which is easily recognized by those with experience of the disease, and is of unfavourable prognosis. As a rule even children are content to lie still in bed without attempting to sit up, and this suggestion of weariness is not by any means limited to severe cases. Even in its mild forms diphtheria, by its toxins, seems to exercise a markedly de-

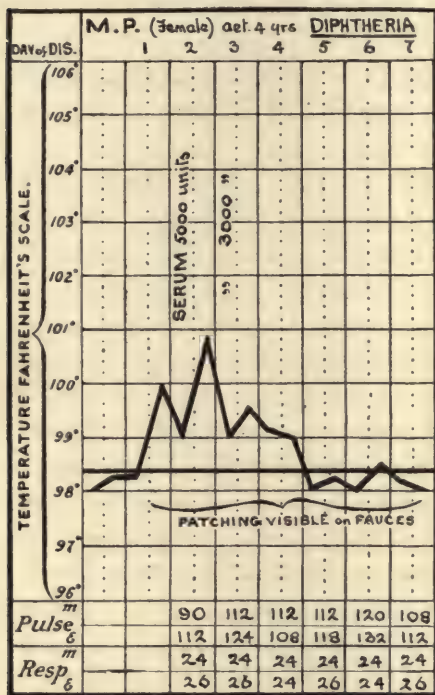


FIG. 46. A case of faucial diphtheria of moderate severity. The first rise of temperature was at midnight, and accompanied by vomiting. A definite, but not large, patch of membrane on one tonsil. This was somewhat persistent, although serum was employed.

pressing effect. We have seen that, as a rule, there is not much pain in the throat, which no doubt accounts to some extent for the remarkable rapidity with which quite young children submit themselves to local treatment. But the almost sedative effect of the toxins on the nervous system must have much to do with the passiveness under treatment which, to my mind, is such a characteristic feature in children suffering from diphtheria. It is rare for these children not to be under perfect discipline within two days. Contrast them with children suffering from scarlatina anginosa, who

in the hands of the selfsame nurses may struggle and fight every time the throat is treated for three or four weeks, and, never resigned to hospital discipline, are constantly attempting to sit up. Many severe cases of diphtheria show great drowsiness, and may require to be roused for every feed. Patients suffering from the milder forms, however, usually preserve their appetite and take their food well, especially after their fever has disappeared. The throat symptoms, even when well marked, seldom cause difficulty in swallowing, and even in the worst forms of the disease the mouth can usually be opened well and without pain.

Albuminuria and the kidneys. In a well-marked case albuminuria is a frequent symptom. When antitoxin was first introduced, it was suggested that this feature of the disease became more common. This, however, is a mistake, and there is no reason to believe that the serum is in the least deleterious to the kidneys. Indeed, as we regard the albuminuria as a purely toxic symptom, directly due to the effect on the renal organs of the toxin circulating

in the blood-stream, we should be justified in assuming that antitoxin would have rather a preventive than a causative action, and this, from my experience of diphtheria before and since serum treatment was introduced, I firmly believe to be the case.

Occasionally renal casts may be found in the urine, but there is little reason to believe that there is any acute nephritis. Blood is very rarely present. The albumin may vary in amount from a faint trace to considerable quantities, the urine in bad cases becoming almost solid on boiling. The amount may vary markedly in the same case from day to day. In averagely severe diphtheria the proportion of patients with this symptom is about 30 or

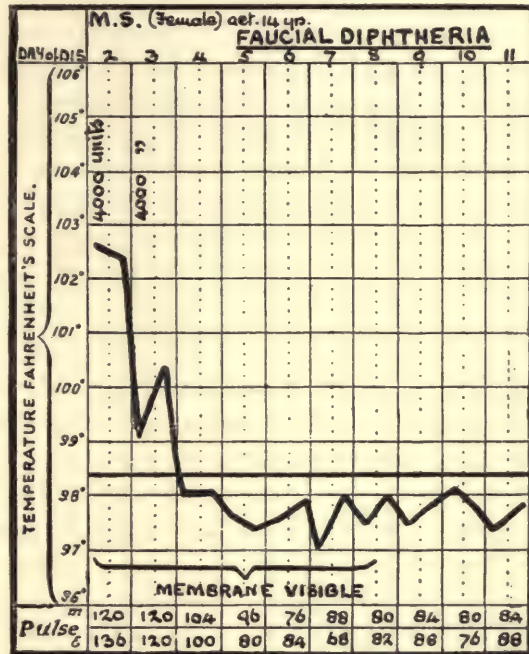


FIG. 47. A sharp case of faucial diphtheria, showing considerable initial pyrexia and thereafter well-marked subnormal temperature.

40 per cent., but, when the epidemic is benign in character, the percentage may be very much less. The symptom is of some importance in prognosis, as practically all bad cases present it. Its absence, then, may be construed as a favourable sign. When it appears, it is chiefly to be found between the fourth and tenth days. Thereafter it seldom makes its first appearance. It does not, as a rule, last long in convalescents, and I do not recollect ever having discharged a case with albumin still in the urine.

The quantity of urine passed in the twenty-four hours varies considerably. In severe cases it may be very much reduced, and occasionally there is absolute *anuria*, a condition which very rarely results in recovery. Goodall, who has made a special study of this question, attributes the diminution in the urine, not to a true nephritis, but to a toxic interference with the nervous mechanism of the kidney, and this would appear the most rational view to hold. This fatal complication is chiefly noticed in very toxic cases with failing hearts, and often appears from twenty-four to thirty-six hours before death.

As regards true *nephritis* I have only seen two or three cases follow diphtheria. The condition was present about a fortnight after the commencement of the attack, and I was able to exclude scarlatina. It is so rare a complication, however, as to need no comment.

Erythematous rashes. It is beyond all question that certain rashes, quite independent of treatment by serum, appear in the course of diphtheria. These were frequently noted in the days before antitoxin was in use, and they may complicate the diagnosis. Different varieties of multiform erythema have been described, but the only rash I am personally acquainted with is a somewhat dusky erythema usually limited to the trunk, but also seen on the flexor surface of the larger joints, and not definitely punctate. It may nevertheless suggest scarlatina. It is comparatively rare and only seen in the early days of the illness. It is more than probable that the forms of erythema described by the French writers were accidental rashes due to enemata, sepsis, and other similar causes such as we still see in septic scarlatina and in enteric. Nowadays if such rashes occur in the convalescence of diphtheria there is nothing to distinguish them from those due to serum.

TYPES OF FAUCIAL DIPHTHERIA. The disease, as it affects the throat, may vary very much in severity both as regards its tendency to extension and as to the amount of toxæmia which it causes. We may distinguish firstly **mild types**, in which there is but little or no local lesion, and practically no toxæmia. The so-called catarrhal diphtheria, in which nothing is seen in the throat beyond slight congestion, may be regarded as

the lightest form in which the infection manifests itself. It may be reasonably asked whether the appearances presented are not merely the efforts of a healthy mucous membrane to throw off the disease and to get rid of the bacilli, rather than a genuine instance of slight infection. The only evidence in favour of the latter is the presence of the Klebs-Löffler bacillus. But we have already seen that it may also exist in apparently healthy throats. Only of slightly more importance are those cases in which patching to a greater or less extent is visible in the fauces, but which present the characters of an ordinary spotted or septic throat. The patch may consist of pultaceous material, easily wiped off, or if it is membranous the membrane is readily detached and breaks up easily. Such cases before the days of bacteriological diagnosis would never have been termed diphtheria. There is seldom much in the way of constitutional symptoms, albuminuria is most rare, and convalescence is rapid. It is quite exceptional to find such throat conditions followed by either paralysis or heart failure, but it would be dangerous to assume that such sequelæ are impossible. Secondly, we may class the great majority of cases of diphtheria as of **moderate type**. In such patients the membrane is definite and firmly adherent. It is usually limited to the tonsils, the pillars of the fauces, and the uvula, and often does not involve the latter structures at all. The glands are moderately enlarged and tender, the patient shows no great amount of prostration except after exertion, and it is not at all unusual to find traces of albumin in the urine. These cases usually recover, but they are liable to the less dangerous forms of paralysis, and, if care is not taken of them, to heart failure in convalescence. Thirdly, we have **severe types**. Of these the most commonly met with is that in which, in addition to the fauces, the upper part of the pharynx and the posterior nares are involved, as evidenced by discharge from the nostrils. The membrane also frequently covers the soft palate. Albuminuria is the rule from about the fourth day, and toxic symptoms are altogether more in evidence. This is accounted for by the large supply of lymphatics to the nasal cavities. The glands are moderately or extremely enlarged and may be very hard. Heart failure may occur early, and the pulse from the first is poor, soft, and irregular. The patient is often extremely drowsy, and is usually very apathetic. The colour is bad, the face being pale and occasionally of a dusky, almost cyanotic, tinge. Even with serum treatment it may be a week or ten days before the throat is clear of membrane, that is to say, if the patient lives so long. The temperature, probably elevated at first, very soon reaches the normal line in these cases, and is often subnormal before the end of the first week. Prostration is the outstanding feature of this and other severe forms of diphtheria.

Closely resembling the above is the **septic type** of the disease, in which either streptococci or staphylococci play a prominent part, in addition to the bacillus. In these patients there is usually more oedema in the throat, a higher and more prolonged temperature, and a greater tendency to the formation of a collar of matted glands round the neck. Nasal discharge is often present, and the ears also may suffer, otitis media with subsequent perforation of the tympanum not infrequently resulting. The membrane in these cases is often remarkably thick and leathery, and the smell from the throat extremely offensive. The oedema and consequent pain on swallowing, and the tendency to suppuration and sloughing on the part of the glands, are apt to counteract the usually soothing effect of the diphtheritic toxin and the patient may be very irritable and sometimes restless. Delirium also is more frequent in cases of this type, which in many ways resembles the septic form of scarlatina. A high percentage of these cases terminate fatally, and it is not to be expected that the full benefits of serum treatment will be obtainable, so much of the toxæmia depending on micro-organisms other than the Klebs-Löffler bacillus.

The most deadly variety of diphtheria is the **hæmorrhagic type**. The intensity of the toxæmia is here sufficient to cause blood changes, which result in hæmorrhages from the mucous membranes and into the skin. There may be dangerous epistaxis, blood oozes profusely from the affected parts of the throat, and definite purpuric spots appear on the surface of the skin. Subconjunctival hæmorrhages are not uncommon, and in two patients I have noticed that the tears were definitely tinged with blood. The tissues bruise easily. In patients with whom no undue force has been used in holding them for the purpose of giving a serum injection, I have frequently noticed the marks of the nurse's fingers on the wrists and thighs. The site of the injection, also, shows much bruising. These patients soon present a waxy pallor and are apt to be restless. The urine is much diminished in quantity and may be entirely suppressed. Large quantities of albumin are present, but hæmaturia appears to be a very rare symptom. I have personally never noticed it. Death invariably occurs, usually well within a week. The throat symptoms in these cases are usually, but not necessarily, severe.

It is obvious that, as in other diseases, it is impossible to expect cases to conform to types. Many patients will be seen whom it is hard to classify under one heading rather than another. For instance, a suggestion of the hæmorrhagic type is occasionally met with in very severe cases, which may show considerable bruising, and may suffer from moderate bleeding from the nose or throat, but which have no purpuric hæmorrhages in the skin.



HEMORRHAGIC DIPHTHERIA.

Skin hemorrhages in a toxic case. The larger patches represent the bruising caused at the site of subcutaneous injections of serum.

Such patients occasionally make a good recovery. Again, a patient may at first suffer from what appears to be only a mild attack, and suddenly, without apparent reason, may assume all the characters of a severe toxic or septic type. Such sudden transitions, however, were more frequently seen in the pre-antitoxin period, and are not to be expected if an adequate dose of serum is administered when the case first comes under observation.

LARYNGEAL DIPHThERIA. The disease may primarily affect the larynx and may be limited to that situation. Or it may spread upwards and downwards, involving the pharynx and fauces on the one hand, and the trachea, bronchi, and lungs on the other. Or, as we have seen, starting in the fauces, it may secondarily involve the larynx. In any case the symptoms of the laryngeal form of the disease are definite and distinct, and must be considered separately. What we now have to describe is the condition popularly known as *croup*.

The term **croup** may be held to cover the symptoms of laryngeal obstruction. If this is due to the presence of a false membrane the case may be regarded for all practical purposes as one of diphtheria. It is true that occasionally membranes are found, the formation of which has apparently depended on the action of other micro-organisms. Such conditions are comparatively rare, and in any case the authorities wisely insist that all cases of membranous croup shall be notified. We cannot do better than adopt the old division of the symptoms into three stages—the initial, the spasmodic, and the obstructive.

1. *The initial stage.* The patient, who may or may not be already suffering from a diphtheritic faucial lesion, shows signs of laryngitis. The voice becomes husky and is often quite lost. Cough is also present, and soon assumes the characteristic metallic ring. It is impossible to give an accurate description of it. It has been compared to a hoarse bark, or the crowing of a cock with a cold. There is no better word for it than 'croupy'. The temperature is usually elevated two or three degrees above normal. The respiration is slightly accelerated and is occasionally stridorous, but at this stage there is no dyspnoea. Aphonia and a frequent cough are, indeed, the outstanding features at this early period.

2. *The spasmodic stage.* After the above symptoms have lasted for a varying time, sometimes for only a few hours, the patient becomes liable to recurrent paroxysms of dyspnoea. These at first may be of only moderate severity, but, in the average case, rapidly become serious. The dyspnoea may commence quite suddenly. The breathing becomes laboured and noisy, with marked inspiratory stridor. The face becomes red and congested. The extraordinary muscles of respiration are called into action. The child tries

to assume an attitude in which he can breathe with comfort, and shifts his position frequently, often trying to sit up. Then perhaps a fit of coughing reduces him to a condition approaching suffocation. He literally fights for breath. The face becomes cyanosed, the nostrils dilate, the rapidity of respiration is increased. He fails to fill his chest on inspiration owing to the obstruction at the glottis, and, as a result, the soft parts of the chest, instead of being pushed out, are drawn in. Above the sternum, in the intercostal spaces and at the epigastrium, this *recession* of the soft parts is noticed. The paroxysm of dyspnœa is at first short, lasting only a few minutes. The patient ultimately gets relief, occasionally after the coughing up of large quantities of mucus which may or may not contain shreds of membrane. After the paroxysm the breathing is often quite easy, the only peculiarities noticed being those characteristic of the first stage. The child, exhausted by the spasm, often drops to sleep at once. After a varying interval, which becomes shorter as the condition progresses, the sleep becomes restless and disturbed, and the breathing more noisy. Ultimately the discomfort is sufficient to wake the patient, and his anxiety and nervousness contribute to the severity of the succeeding paroxysm. These accesses of suffocation probably depend for the most part on spasm of the glottis as the result of the irritation caused by the presence of membrane in that situation. When the patient is apparently at his worst, and is thoroughly exhausted by the laboured breathing, the spasm is apt to relax. The coughing, however, may partly or completely detach pieces of membrane, and the patient may die of purely mechanical obstruction if the loosened membrane sticks at the glottis.

As the paroxysms become more frequent and more severe, the patient begins to obtain much less relief in the intervals. The difficulty in breathing becomes more continuous, the recession of the intercostal spaces being noticed even after the spasms are over. Restlessness becomes well marked and continuous. This is the beginning of the third stage.

3. *Stage of permanent obstruction.* The patient gets more and more exhausted and the membrane has probably increased in amount sufficiently to be the cause of mechanical obstruction to the breathing. No doubt also by this time the œdema in the neighbourhood of the glottis, which plays a great part in the obstructive process, has become much more marked. The dyspnœa is now permanently present. Cyanosis is constant, and the pulse shows marked signs of failing, becoming small, irregular, and often extremely rapid. Hitherto, especially in the intervals, it may have remained reasonably good. This is especially true of purely laryngeal and tracheal cases. When faucial and nasal lesions are also present there is more toxæmia,

and, as a result, the heart fails earlier. The recession of the intercostal spaces and of the epigastrium is constant and at first well marked, the latter sometimes being drawn so completely in as to leave a hollow, almost the size of a small teacup, on inspiration. But as the patient's strength fails, and the force of the respiratory efforts diminishes, the chest is less fully dilated on inspiration, and as a result recession may become much less marked. With the gradual failure of the heart, the face, at first congested and cyanosed, becomes pale and livid. The lips are purple and may be slightly swollen, and the restlessness which has been such a marked feature since the end of the second stage may now cease altogether, the patient being too prostrate to struggle. This, the last stage of many untreated cases, constitutes the 'asphyxie blanche' of the French writers.

It is obvious that all cases cannot be expected to develop in the same manner. Some children, after a brief first stage, die in their first paroxysm, from obstruction with a plug of membrane, or from acute œdema of the glottis. Others may suffer from a dyspnœa progressively growing worse, and comparatively free from spasmodic exacerbations. This is the usual course of the condition in adults, in whom, it may be remarked, implication of the larynx is rare. Some adults may have laryngeal diphtheria with no worse symptom than a little hoarseness, and yet cough up complete casts of the larger air-passages. It is easy to see how membrane of a given thickness may hardly inconvenience an older person, and may yet seriously contract the available breathing-space of a child.

Diphtheria of the trachea. We occasionally meet with cases in which the voice remains unaffected and the cough is not, strictly speaking, croupy, but in which signs of obstruction are well marked. Many of these are probably tracheal. In any case the glottis has escaped inflammation and exudation. Complete casts of the trachea, with sometimes bronchial casts also, may be coughed up. In these cases the dyspnœa is progressive and not paroxysmal. The smaller bronchi are frequently involved, and diphtheritic broncho-pneumonia may supervene. The noise in the trachea and bronchi often makes satisfactory auscultation of the chest quite impossible.

In the laryngeal and tracheal forms of diphtheria the temperature usually remains elevated. Particularly is this the case if the lungs become involved. On the other hand, and especially in cases in which faucial or nasal lesions also exist, the temperature may remain consistently normal. The respiration is sometimes only slightly accelerated. In pneumonic cases, however, it is always extremely rapid. Any enlargement of glands depends rather upon lesions in the throat or nose. If these are absent there may be no adenitis

at all. Broadly speaking, when the disease is entirely limited to the larynx and trachea, there is but little toxæmia, and, once the danger of suffocation is over, convalescence is usually uninterrupted. Albuminuria is not very common, and late heart failure and paralysis are both very rare. This, no doubt, depends on the peculiar arrangement of the lymphatic vessels of the larynx, which, it will be remembered, form a plexus of their own, and have but little direct communication with the general lymphatic system, as is evidenced clinically by the rarity with which metastatic growths follow malignant disease in this situation. There is not, then, the same chance of toxins being absorbed from lesions in the larynx, that there is when the disease affects the nose or fauces.

NASAL DIPHTHERIA. Various types of this condition have been described, and it is not always easy to class any given case under any particular heading. In my experience, cases of diphtheria affecting the nasal cavities may be roughly divided into three groups. *Firstly*, we have the large group of cases in which the fauces or pharynx are involved as well as the nose. The primary lesion may be in the posterior nares, or the infection may have spread to that situation from below. As regards the nose itself the lesion may be limited to the nasopharynx, or may also be present in the anterior nares, membrane being visible in the nostrils. More commonly, any membrane that may be present is limited to the posterior fossæ of the nose, and its presence is indicated by discharge from the nostrils. This discharge is usually clear at first, but after a day or two it becomes sanguineous or purulent, and there may be attacks of epistaxis. Occasionally shreds of membrane are noticeable in the discharge, and more rarely large casts of the nasal fossæ may be dislodged by douching. Even if the faucial or pharyngeal lesions are slight these cases are extremely serious. There is much toxæmia, often early heart failure, and a high percentage of the cases subsequently develop various forms of paralysis. I regard it as by far the most fatal form of diphtheria, always excepting cases which are definitely hæmorrhagic.

Secondly, the lesion may be entirely limited to the nose. The first symptoms are usually a blocking of the nasal passages, with much snuffing and mouth breathing. This is early followed by muco-purulent discharge, which may be very profuse, and is liable to excoriate the nostrils and lips. The submaxillary glands are usually enlarged. Definite membrane is present in the nose, and may be occasionally visible if the nostrils are carefully examined. The severity of this type of diphtheria varies greatly. Some cases show as much toxæmia as the preceding group, but this on the whole is rare, as we would naturally expect that, if the infection was virulent, the pharynx

would be attacked by the membrane before the nature of the disease in the nose was suspected, and appropriate treatment employed. The mere limitation of the membrane to the nostrils would point to a moderate infection. Many cases are of the type described as 'fibrinous rhinitis', which, though it often depends on the diphtheria bacillus, and may last for a long time, is not accompanied by severe constitutional symptoms. In young children, however, constitutional disturbance may be well marked, even when the membrane is limited to the nose, and such cases must always be regarded seriously, as they may be followed both by heart failure and paralysis. When, on the other hand, there are no signs of a general infection, and the local condition is all that can be observed, the mere fact that membrane is present is the only feature which distinguishes the case from the third group now to be mentioned.

Thirdly, then, there are cases in which there is nothing more than discharge, and often a very trivial discharge, from the nose. I do not regard such patients as suffering from diphtheria. They are, however, hosts of the bacillus, and are therefore dangerous to other people. They present no constitutional symptoms whatever, and the most careful and prolonged syringing fails to dislodge anything like membrane from the nose. The bacilli present in the discharge are not by any means always pathogenic to guinea-pigs, but they are morphologically, and in culture, indistinguishable from the diphtheria micro-organism, and not infrequently they are beyond all question virulent. Cases of this sort may harbour the bacillus for months, with no visible symptoms beyond a 'dirty nose', and may communicate the disease to persons with whom they are in contact. I have on several occasions seen outbreaks occur in the wards of a children's hospital as the result of patients with such discharges being admitted for some other cause. The discharge is often intermittent, sometimes stopping for days together, and as, beyond causing the discharge, the bacilli produce no ill effects, it is easy to see how these cases often remain unrecognized. Many of the cases of rhinitis following scarlet fever appear to be of this type and due to the diphtheria bacillus.

We have, then, in the above description some explanation of the extraordinary variety of opinion expressed regarding the gravity of nasal diphtheria. When once it has obtained a lodgement in the nose the bacillus may be responsible for either the most serious or the most benign forms of the disease, if, indeed, it is to be admitted that persons suffering only from a nasal discharge containing bacilli are in reality cases of diphtheria and are not merely carriers.

DIPHTHERIA IN OTHER SITUATIONS. Other situations than those already mentioned may be affected, sometimes primarily, though more often as the result of a secondary infection from the throat or nose. A comparatively common site for secondary infection is the **vulva**, which is frequently inoculated by the fingers of a child, who has possibly already been picking her nose. A typical membrane may form on the labia minora, and may spread extensively, adding much to the toxic risks of the case. The lesion in this situation, however, is sometimes primary. I have seen it complicate the puerperium in a patient who was entirely free from other manifestations of diphtheria. In addition to the presence of the membrane there is usually a moderately profuse purulent discharge, which excoriates the surrounding skin. If the patient scratches herself much, there may be many unhealthy-looking sores in the neighbourhood of the part. In small boys the **prepuce** may become inoculated in a similar manner, and I have seen a definite grey membrane spread all over the glans penis. The only case in my experience in which the disease was primary in this situation occurred after a circumcision, and so must be more properly classed as wound diphtheria. In one case I have seen a primary lesion of the *anus*.

Diphtheria may also affect the **conjunctiva**, and here also the lesion may be primary or secondary in character. If the former, it is sometimes caused by a patient coughing directly into the face of an attendant. If the latter, it is most likely to occur in patients who suffer from nasal diphtheria. Two varieties occur. Firstly, the croupous form, in which the lesion is superficial, a membrane which it is not very difficult to detach appearing on the inner surface of the lids. The ocular conjunctiva is congested only, and the lids, though swollen, can be fairly easily separated. Secondly, there is the so-called interstitial form in which the bacillus causes an infiltration of the lids and the surface of the eye itself, with profuse straw-coloured discharge. The lids are enormously swollen, and it is often impossible to separate them. The cornea may slough and the eye be destroyed. I have only seen one case of this description. The diphtheria bacillus was present, and some membrane was visible, but the nature of the case was even more fully proved by the mother taking faucial diphtheria a few days later. The child suffered from only slight constitutional symptoms and escaped with the loss of sight of one eye. It must always be remembered that other conditions besides diphtheria may cause croupous inflammations of the conjunctiva, and the mere presence of a suspicious-looking membrane is no certain evidence of the presence of the disease. Moreover, the xerosis bacillus is a diphtheroid organism which it is extremely difficult to differentiate from that of diphtheria.

We have seen that in some cases of faucial diphtheria the membrane may attack the inner surfaces of the cheeks and lips, though the former of these situations is distinctly rare. In some cases, especially it is said after measles, **buccal** lesions may be the first signs of the infection. Both the *tongue* and *lips* may suffer, soft aphthous-looking patches appearing on the former. The membrane in this situation seems very resistant to treatment. This no doubt is due to the fact that such lesions are seldom seen except in cases of mixed infection, usually streptococcal, and therefore are unlikely to benefit fully by the use of serum. Another unusual site for diphtheritic infection is the *external auditory meatus*, the lesion being usually secondary. This variety of diphtheria I have only seen on one occasion.

Among other unusual situations we may mention the *oesophagus*. Rolleston was able to discover records of 22 cases of this rare localization. Occasionally a cast may be expelled, but this seems to be unusual and ordinarily there is ulceration at the site of the lesion and a very considerable risk of subsequent stenosis. Membrane has been found in the *stomach*, and ulceration of the *duodenum* depending upon diphtheritic infection has also been reported. Cargin has observed a case in which diphtheritic enteritis was present and a cast, six inches long, of some part of the small *intestine* was passed in the stools.

Considerable attention has lately been given to **cutaneous diphtheria**. Perhaps it would be more logical to regard this form of infection as wound diphtheria, as probably some slight abrasion is always present. In one group of three children I have seen patches of redness on the skin of the abdomen and thighs, with here and there a greyish appearance but no definite membrane, from which pure cultures of the bacillus were obtained. The most marked lesions were in the groins, and the bacillus had probably been assisted in obtaining a nidus by the presence of some degree of intertrigo. Other cases have been reported in which the skin condition resembles impetigo contagiosa and is associated with conjunctival or nasal discharge. Cases of eczema and other skin disease may become infected with diphtheria and, while membrane may occasionally be recognized, it is by no means invariably present. Such an infection, if undiagnosed, may cause symptoms for many months.

Lastly must be mentioned diphtheria infecting **wounds**. An abraded surface may become inoculated, and may present a definite membrane. Occasionally, however, the infection merely causes the wound to take on an unhealthy action, and a dirty sloughing surface is the result. The true nature of such lesions is sometimes made clear by the patient subsequently developing definite post-diphtheritic paralysis. I have seen at least three such

cases in which there was no other lesion, either in the fauces or elsewhere. But secondary infection of wounds, usually from a pre-existing rhinitis, has not been very uncommon in my experience. Recently numerous cases of wound infection, many with resulting paralysis, have been seen in military hospitals, and it is probable that many more have not been recognized.

THE HEART AND CIRCULATION IN DIPHTHERIA. If we exclude broncho-pneumonia, which is in laryngeal cases a common cause of death, circulatory failure is undoubtedly responsible for the greatest number of deaths in diphtheria. In every case there is the possibility of heart trouble arising, and from the first the pulse must be carefully watched. At the outset, as we have seen, it is rapid, soft, and compressible. In mild cases it slows down as the temperature falls, but still remains soft. Towards the end of the first week in an averagely severe case it not unusually becomes somewhat irregular. At about this period, also, it may cause alarm by becoming either unduly fast or unduly slow. Either extreme may denote the onset of serious cardiac trouble, but in some adults the pulse may remain in the neighbourhood of 50 for several days without any evil result. In very severe cases, where there is much toxæmia from the start, the pulse commonly remains rapid, often exceeding 140 in young children. The irregularity is well marked, and is noticeable both as regards the strength and the rhythm of the wave. Thus a well-marked beat may be succeeded by several feeble ones in rapid succession, or well-marked gallop rhythm may be observed. Occasionally there is intermission, a beat being missed at more or less regular intervals.

As regards the heart itself, soft systolic murmurs may be heard in many cases, not necessarily among the most severe. In severe cases reduplication of the second sound is often heard on auscultation at the base, and the first sound may be very faint. Endocarditis is very seldom present, and, should it be so, is probably due to other micro-organisms than the Löffler bacillus. As regards the *blood pressure*, Rolleston found it was lowered in 35 per cent. of his patients, 'the extent and duration of the depression having, as a rule, a direct relation to the severity of the faucial attack'. The lowest readings were found in the second week of the disease.

Recent work with polygraphic tracings by Gunson, Hume, Clegg, and others has thrown some light on the defects of cardiac action and, it is sincerely hoped, will ultimately, when further developed, assist in devising some method of treatment. Arrhythmia is a frequent phenomenon in diphtheria, and Gunson has assisted our prognosis by his observation that the so-called sinus arrhythmia, the quickening of the pulse during inspiration and slowing on expiration, which in well-marked cases may give an impression

of great irregularity, is not of practical importance and need not detain a patient in bed after the fourth week. On the other hand, arrhythmia associated with dilatation, gallop rhythm, and hepatic enlargement is of very grave significance. Many irregularities of cardiac action have been noted; premature auricular contractions, premature ventricular contractions, auricular fibrillation, heart block, auricular flutter, nodal rhythm, and reversal of the normal beat all figure in the literature. Unfortunately few of our fever hospitals are so staffed as to be able to give this subject the attention it undoubtedly deserves, and it is satisfactory to learn that Rolleston considers polygraphic methods do not tell us much that cannot be suspected by clinical examination.

In considering **cardiac failure**, or cardiac paralysis as it is sometimes called, we are at once confronted with certain difficulties regarding its causation. It has been attributed to myocarditis, to vagus degeneration, to changes in the medulla, and to suprarenal insufficiency. As regards the latter theory there is much to be said for the view that a certain number of deaths among severely poisoned cases of diphtheria and other acute diseases are due to a failure of function on the part of the suprarenal glands which undoubtedly may present hæmorrhages and degenerative changes both in the cortex and medulla. On the other hand, the degeneration of the myocardium is so well marked in many fatal cases that it does not seem reasonable to exclude the probability of this lesion being often the real cause of death, though we may admit with Baginsky that in certain cases the myocardium seems almost unaffected. Gunson, whose painstaking work on the subject entitles him to an authority to which I cannot pretend, holds that clinical observation is all in favour of a nervous origin of the failure in those cases in which the vascular system is not at fault, and points out that it is agreed that in post-diphtheritic paralysis the nerve and not the muscle element is the source of trouble. It is undoubtedly the fact that marked degeneration of the vagus has been observed fairly frequently, and the clinical picture in many fatal cases certainly points to that nerve being involved, and in the case of late heart failures it is not uncommon to find associated with it paralysis of muscles supplied by other cranial nerves such as the phrenic or spinal accessory. Personally I believe that all these factors may play some part in the production of heart failure, and I have hitherto considered that in the early cases the myocardium is chiefly at fault, while the later ones partake more of the nature of a paralysis. Gunson's classification has compelled me to revise these views, and my experience has been that a large number of cases fall naturally enough into the two groups which he has described. In the first of these he considers the *vascular*

system at fault. 'The cardiac rhythm remains normal and there is a primary failure of the peripheral circulation with subsequent embarrassment of the cardiac action.' The symptoms are vaso-motor and depend on disordered nervous function, the suprarenal glands playing an important part. His

second group, the *cardiac*, is associated with arrhythmia and tachycardia, and may be regarded as a cardiac paralysis.

As has been said above, heart failure may occur early or late in the illness, and many of the former group will be found to conform to the vascular type described by Gunson. *Early heart failure* may occur at almost any time in the first fortnight of the illness. It is usually progressive, that is to say, the pulse is bad from the first and gets almost imperceptibly worse. Occasionally, however, the failure occurs with startling suddenness. The patient has usually suffered from more than averagely severe throat lesions, and in the vast majority of my cases there has been discharge from the nose as well as membrane in the throat. From the first there has been evidence of profound toxæmia, and such symptoms as prostration, drowsiness, and pallor have been

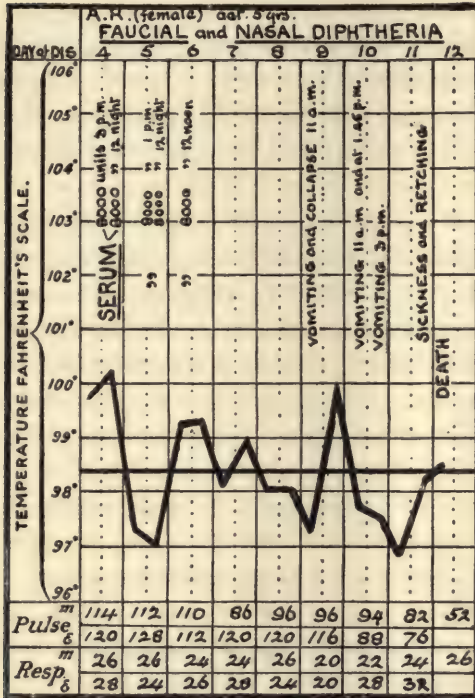


FIG. 48. A severe case of naso-pharyngeal diphtheria. Serum pushed at first till 40,000 units had been given. Hæmorrhage from nose and throat, and purpuric spots on the skin. Ecchymoses. Note the low temperature, often subnormal, and the slowing pulse. Death from toxæmia and progressive cardiac failure on the twelfth day.

prominent. The urine has been loaded with albumin, and often very much diminished in quantity. The pulse has remained as a rule rapid, and its rapidity has often increased, even when the temperature has come down to normal or subnormal. It may also have been irregular and, after the first few days, difficult to feel at the wrist. By the end of the first week, or even earlier, the extremities have become cold, and a tinge of cyanosis is often visible in the complexion. The heart may or may not show dilata-

tion and often there is little to be made out by auscultation. The liver dullness is in some patients much increased, but this is not very usual in this type of case. Finally comes syncope, the patient becoming blanched and apparently lifeless. Not infrequently he may rally from his first fainting fit, but in these progressive cases, which have shown bad symptoms from the start, the improvement is only temporary. With the first signs of the final change, sometimes before the syncope, there is a tendency to vomit, and, as a rule, nothing will lie in the stomach. Sometimes there is præcordial pain, though I think hardly so frequently as in the sudden cases which occur in convalescence. The patient remains almost pulseless, the hands and feet stone cold, the face livid and sometimes covered with cold sweat, and he either gradually passes away or, more usually, fails to rally from one of the recurring attacks of syncope. We have seen that drowsiness is often noticed during the earlier stage; when once fatal symptoms have set in, the mind occasionally becomes unnaturally acute, and consciousness is maintained to the last, the end not infrequently occurring in a convulsive seizure.

Cardiac failure may also occur unexpectedly in the first fortnight of the illness in patients who have not manifested such a marked toxæmia from the onset. Sometimes there may be a direct cause for this, such as undue exertion or undue strain. I remember particularly the case of a girl with most moderate faucial lesions, who, in the first week of her illness, died in the ambulance removing her to hospital. She had dressed and remained sitting up waiting for it for over an hour. Again, while performing intubation the insertion of the gag may cause a fatal collapse, and some deaths on the table during tracheotomy are undoubtedly due to sudden failure of the heart. I have also seen straining on a bed-pan cause such marked symptoms of cardiac failure that the patient was in the greatest peril for four days. But, apart from any undue exertion, heart failure occurs sometimes quite suddenly even within the first ten days of the illness, and before there are any signs of paralysis, except, perhaps, that precocious paralysis of the palate which is a bad sign in diphtheria, and which is so often associated with early cardiac failure. In such cases there has often been much albumin in the urine.

Late heart failure may occur at almost any time in convalescence. It is probably largely due to changes in the vagus, and occurs during the period at which paralysis is commonly met with. It may declare itself in cases of generalized paralysis very late in the disease. As long as the paralytic symptoms continue the patient is not safe. On the other hand, it seldom appears after the end of the fourth week, if up to that time the patient has

not shown any sign of paralysis. I have, nevertheless, seen it in the sixth week in a patient who had manifested no paralytic symptoms whatever. Doubtless the condition of the cardiac muscle often assists in the process, and the pulse has seldom been really satisfactory before the failure occurs. But there is not the same suggestion of gradual progression to a fatal termination that there is in the early cases, and the first really serious symptoms occur with very little warning, often in patients the condition of whose pulse, though not very good, may have nothing to distinguish it from that of half a dozen other patients in the same ward.

The first sign of this dangerous condition may be a sudden change in the rapidity of the pulse. If a patient, whose pulse has remained about 100 for some time, is found to have a pulse of 80 or 120, there may be trouble in store. Usually the first obvious symptom is an attack of vomiting. Sometimes, however, pain is complained of before anything else. The pain is often præcordial, but by no means invariably so. It is frequently referred to the abdomen and sometimes to the extremities. In one case in my recollection it was so definitely referred to the area of the appendix that the patient was carefully examined for appendicitis, her anxious expression and acute mental condition being quite suggestive of some abdominal inflammation. In young children it is often difficult to find out where the pain is. They obviously suffer intensely and have, no doubt, a sense of oppression which they cannot explain. As a result, restlessness is often a marked symptom in these cases. Either with the vomiting and pain, or shortly afterwards, syncope occurs. The patient faints and becomes pulseless. As a rule, if prompt measures are taken, he survives the first collapse and may live for three or four days. During this time the vomiting continues at intervals, and the pain and præcordial anxiety persist. The patient is deadly pale, his lips cyanosed, his expression anxious. The breathing is often laboured, with irregular respirations. The extremities are cold. The pulse is extremely weak, irregular, and may be very rapid. The temperature is often one or two degrees below normal. The liver usually shows enlargement and sometimes reaches to the umbilicus.

The most distressing feature of this terrible sequela of diphtheria is the acutely conscious mental condition of the patient. His sufferings, which are often very severe, are not in the least blunted. He talks coherently and sensibly to the end. He can find ease in no position for more than a few minutes, and is continually shifting himself in bed, or, when too weak to do so, asking to be moved. He is often tortured by thirst. Any fluids given by the mouth are promptly returned, and rectal or subcutaneous injections of saline fluid only give him very temporary relief at best. The pain is often

of the most agonizing character, and children often moan continually and sometimes actually scream. The end usually comes by a sudden syncope, often just after an attack of vomiting or retching.

In some cases death occurs with startling suddenness. A child, who may or may not have suffered previously from some form of paralysis, sits up in bed and falls back dead. But, as has been said above, after the first collapse it is usual for the patient to live at least a few hours, and more often some days. Death is not inevitable. I have seen patients who had, in a modified degree, all the three dangerous symptoms, pain, vomiting, and syncope, ultimately recover, but anything except a fatal termination is most unusual.

POST-DIPHTHERITIC PARALYSIS. This condition, depending on degeneration of the nerves caused originally by the toxins of the disease, does not, as a rule, manifest itself until after the first fortnight of the illness. We have seen, however, that the cardiac nerves are sometimes affected early, and in severe cases it is not uncommon to see an early paralysis of the palate. The paralysis is fortunately seldom complete, and is in most instances more strictly a paresis. Many of the nerve fibres seem to remain unaffected. The condition is most frequently met with in cases of more than average severity. It may, however, follow what has apparently been a very mild infection, and particularly is this the case if the disease has been unrecognized and therefore untreated. In my experience it is in patients who have presented both faucial and nasal lesions that paralysis is most frequently seen. In a considerable proportion of cases the original lesion has been confined to the fauces and pharynx, and in these it will often be found that the uvula, palate, or posterior pharyngeal wall have been involved. I have, however, seen well-marked paralysis follow a slight follicular infection limited entirely to the tonsils. It is most rare to find paralysis in a patient whose lesions have been completely restricted to the larynx and trachea. Broadly speaking, the younger the patient the greater the liability to develop paralysis.

While the generally accepted view of the *pathogenesis* of this condition has been that the toxin in the circulating blood acts, presumably selectively, on certain nerve nuclei, chiefly those of the cranial nerves but also those in the cornua of the spinal cord, and that degeneration of some of the nerve fibres results, Walshe adopts the theory that the toxin is carried directly from the infective focus along the perineural lymphatics. His experience of an epidemic of paralysis following cutaneous infection led him to this conclusion, the situation of the paralysis in his cases having been determined by the situation of the infected sore. It is undoubtedly the fact that the innervation of the palate, fauces, and pharynx is derived from the nuclei of the cranial nerves which most frequently suffer, the

glosso-pharyngeal vagus-accessorius group, but this does not appear to explain paralysis of the oculomotor or ciliary variety, nor does it account for the palsies of the upper and lower extremities following naso-pharyngeal diphtheria. Walshe regards ciliary paralysis as a manifestation of the selective affinity of diphtheria toxin for certain elements of the nervous system, in which, it would seem, he should also include the oculomotor centres and spinal nuclei. Again, palatal paralysis has in my experience occurred in more than one case in which there was no pharyngeal lesion, and the palate, therefore, sometimes is 'selected'. While Walshe's cases certainly suggest that, as in tetanus, the poison is sometimes carried by the lymphatic route, we cannot in the meantime accept his explanation as entirely satisfactory.

The paralysis may be limited to one situation, as for instance the palate or it may affect many parts of the body simultaneously or successively. Not infrequently we see a marked improvement in one situation, followed by the implication of quite a different set of muscles. The general tendency of the neuritis is unquestionably towards rapid cure. If vital parts are left unaffected the prognosis is always extremely good, so far as the recovery of a lost function is concerned. In some sites, the pharyngeal and respiratory muscles especially, the paresis is very short lived. In others, such as the palate, and to a lesser degree the extremities, the loss of function may last for many weeks, or even months.

As regards the *frequency* with which paralysis occurs, it has been suggested that it has been seen much more frequently since serum treatment was introduced. This may be true, though there is reason to believe that the great interest taken in the disease in recent years has stimulated more accurate observation, and that cases are nowadays recognized which some years ago would have been missed. But, apart from this, the great fall in the case mortality implies that a larger number of severe cases recover, and these may be expected to be of the type in which paralysis is likely to be found. It is suggested, moreover, that the nerve changes are due to the action of the toxones, of those bodies contained in diphtheria toxin, in fact, for which antitoxic serum has the least affinity. Our belief in the use of serum treatment, then, need not be in the least shaken by the fact that so far it has failed to reduce the percentage incidence of paralysis. The actual frequency of the condition varies much in different outbreaks. In Edinburgh the percentage has occasionally been as low as 6 and as high as 18. Of the last 9,155 patients admitted with diphtheria to the City Hospital, 915, or just 10 per cent., subsequently developed paralysis. This is probably an understatement, as in young children and infants it is quite possible that

paralysis affecting the ciliary muscle and the lower extremities is frequently missed. The figures, moreover, do not include instances of cardiac paralysis unaccompanied by any other paralytic manifestations.

Palate. The situation most frequently affected is the soft palate. Of the 915 cases mentioned above, 700 were instances of palatal paralysis, and in 328 of these the palate was alone affected. In the other 372 it suffered in conjunction with one or more other muscles, paralysis occurring in numerous different combinations. Of these the most frequent were paralysis of the palate and ocular muscles, of the palate and lower extremities, and of the palate and ciliary muscle. In many instances the palate weakness was associated with what might be fairly described as generalized paralysis, three to seven different muscles being at the same time, or successively, involved.

Palatal paralysis is the earliest of all the forms of muscular weakness to make its appearance, that is, if we except cases of early cardiac failure. It has been observed on the fourth day, and in perhaps one quarter of the cases makes its appearance before the end of the second week. Occurring at this early stage it has been termed 'precocious', and there is good reason to believe that, as is the case with the heart, the palatal weakness depends on local changes in the muscle, a myositis. The frequency with which it appears in patients who have presented severe lesions affecting the palate and uvula goes far to support this view, especially when unilateral paralysis follows unilateral lesions. On the other hand, cases occurring later in the disease may, no doubt, depend on degeneration of the palatine nerves, a condition, indeed, which has been described as occurring so early as the second week. Precocious palate paralysis, in spite of opinions to the contrary, must be regarded as a sign of a more than averagely severe case, and it is often followed by cardiac failure and the graver forms of paralysis. This has been made clear by the valuable work of Rolleston in connexion with this subject, and I may add that it entirely coincides with my own experience.

Of 30 recent patients who developed palatal paralysis in the first fortnight of the illness 14 died, while of 9 of them whose symptoms appeared before the eighth day 7 terminated fatally.

The paresis of the palate is evidenced by loss of function. There is some difficulty in deglutition, fluids particularly tending to be returned by the nose, owing to the failure of the palate to close down properly in the act of swallowing. This regurgitation of fluids is, however, only seen in well-marked cases, and even in these it can often be obviated by the patient taking only small mouthfuls and exercising care. The other most prominent symptom is a nasal twang in the voice, the palate allowing air to escape by the nose at the wrong moment. This may be often noticed quite easily, but

in slight degrees of paralysis it may be advantageous to get the patient to utter test words and sentences. I have been always accustomed to use those suggested by Professor Wyllie. Thus, instead of 'Billy Button bought a buttered biscuit', the patient will say, 'Milly Mutton mought a muttered miscuit.' He is also apt to change d's into n's. Some patients, however, can, as the paralysis is only partial, pull themselves together to pass this test, especially if they are not excited or fatigued by being ordered to repeat it rapidly several times. In such cases, with children particularly, a sentence such as 'Kimball Campbell kicked his kinsman's cattle', by concentrating all their efforts on the correct pronunciation of the first letters, brings out admirably the slurred character of the remaining sounds. The ordinary reply of the Scottish convalescent in hospital, when asked after his health, is, 'Fine, thank you', and this also shows the characteristic twang very well.

TABLE D
SHOWING THE DATE OF ONSET OF PARALYSIS

<i>Muscles affected.</i>	<i>1st week.</i>	<i>2nd week.</i>	<i>3rd week.</i>	<i>4th week.</i>	<i>5th week.</i>	<i>6th week.</i>	<i>7th week.</i>	<i>8th week.</i>	<i>9th week and after.</i>	<i>Totals.</i>
Palatal	10	42	34	25	31	44	8	1	2	197
Ocular-motor	—	6	7	8	5	15	16	6	5	68
Lower Extremities	—	—	—	1	1	3	3	4	14	26
Upper Extremities	—	—	—	—	1	—	—	—	1	2
Ciliary	—	—	—	3	3	4	3	1	—	14
Pharyngeal	—	1	—	—	8	18	12	3	—	42
Neck and Back	—	—	—	—	1	1	2	—	1	5
Facial	—	—	—	—	1	2	1	2	1	7
Respiratory	—	—	—	1	—	2	2	2	—	7
Mastication	—	—	—	—	—	—	1	—	—	1
Laryngeal	—	1	—	—	—	—	—	—	—	1
Palpebral	—	—	—	—	1	—	—	—	1	2
Totals in each week	10	50	41	38	52	89	48	19	25	372

Record of the date of onset of different forms of paralysis affecting 317 individuals out of 3,422 consecutive cases. It is, of course, probable that many cases of lower extremity paralysis were missed, and that the onset in those noted was much earlier than the table shows. The number of ciliary cases is also in all probability much understated. The other figures may be accepted as accurate. Note the concentration, especially of pharyngeal cases, about the sixth week.

On examination of the throat, the palate in a bad case is seen to hang flaccid and immobile, and, if touched, no reflex is present. Occasionally the paresis is only unilateral, a fact which supports the view that the cause of the condition lies in the direct intoxication of the muscle. As a rule, however, both sides seem to be equally affected. It is of importance that even

slight degrees of paralysis should not be missed, and all patients should be tested at intervals. There is no doubt that, once palatal paralysis has occurred, there is a very fair chance of other varieties of paralysis appearing later, and early recognition of the condition will therefore influence both prognosis and treatment very considerably. The paralysis may sometimes last a very short time, a week or ten days, but on the other hand it occasionally persists for months. The patient indeed sometimes talks with a nasal twang for years afterwards, having probably got into a slovenly habit of talking, for there is little reason to believe that the actual muscle or nerve lesion is permanent.

Paralysis of the lower extremities. This is probably the most frequent form of paralysis after that of the palate. In my series of cases it occurred 273 times, and in 84 instances was the only paralytic manifestation. It is probably even more common than this, as only obvious cases were included, and in many instances it is possible that the condition ran its course while the patient was yet in bed. The paralysis is occasionally complete, the legs failing absolutely to support the body. In other cases an ataxic gait, accompanied by loss of reflexes, is the only sign. The patient drags his feet, or sometimes one foot, and tends to walk with a broad base, the legs being somewhat far apart. He often finds turning round a matter of some difficulty. The knee-jerks are usually completely abolished, although in the early stages, or as recovery commences, they may be actually exaggerated. The plantar reflex is absent. There is usually some degree of analgesia, or paræsthesia, it being often quite possible to run pins deeply into the limbs without the patient being conscious of it. Sometimes the legs are quite anæsthetic. A moderate degree of wasting is frequently present, and the muscles are very flabby and soft. It may be assumed that this variety of paralysis usually starts in the fifth or sixth week of illness, but as the table shows it is often not recognized till later. It may persist for some weeks, although complete disability seldom lasts longer than a fortnight.

Paralysis of the ciliary muscle. Loss of the power of accommodation is a very frequent sequela of diphtheria, and perhaps should be placed next to palatal paralysis in frequency. In my series it was noted on 119 occasions, and in 12 of these no other variety of paralysis was present. But it must have occurred much more frequently than the figures indicate, it being extremely difficult to prove its existence in children too young to read. When an attempt is made at reading the patient often makes a good start, but almost immediately the letters become blurred and he can see nothing. The pupil is often somewhat dilated. It is sometimes possible to test the sight of children unable to read by setting them to thread beads.

But unless they have been accustomed to do this before it is not unlikely that wrong deductions may be drawn. Moreover, this test, also, is not practicable in very young children. Ciliary paralysis varies considerably in its time of onset, but is one of the comparatively early varieties, and may be seen in the third week, although it often occurs very much later, even in the seventh or eighth. I have seldom seen it persist longer than five weeks, and its duration is usually much shorter. Perhaps three weeks would be a good average.

Paralysis of the ocular motor muscles. This is usually a sixth nerve paralysis, the muscle most frequently affected being the external rectus on either one or both sides. The internal rectus sometimes suffers, but much more rarely. The result of the paralysis is an obvious strabismus, and the patient may suffer from double vision. In my series this variety was observed 255 times, and on 68 occasions one or other of the recti was the only muscle affected. As the squint is usually easily seen, it is probable that few examples of this form of paresis were missed, even in the youngest patients. While it may occur comparatively early, in the majority of cases it appears in the sixth and seventh weeks, and has usually passed off in about 21 days.

Paralysis of the pharynx. The pharyngeal muscles concerned in the act of swallowing are involved with comparative frequency. This variety is of the greatest importance, as it is in itself a source of danger to the patient, who, if not carefully watched, may choke suddenly and die. One hundred and thirty cases of my series showed pharyngeal paralysis, and in only seven of these was it the only paralytic manifestation. In a few others it was associated with palatal paralysis only, and in the remainder the paralysis was more or less generalized. Association of pharyngeal disability with respiratory paralysis is relatively common, and in my experience the latter is likely to appear in about one-sixth of the cases.

The principal symptoms are a tendency to cough and splutter on attempting to take food, and inability to swallow. Fluids or solids may get into the larynx, and as a result there may be either complete and sudden blocking of the respiratory passages, or a pneumonia, as the result of particles of food reaching the lungs. In one such case, which I remember, the patient died five months later of pulmonary tuberculosis, the ultimate result of the 'food' pneumonia. A great source of discomfort is the inability of the patient to swallow his saliva, which tends to collect in the back of the throat, where it helps to excite the cough. Aphonia is commonly observed, and adductor paralysis is probably not infrequently present.

In the more severe forms of diphtheria the pharynx may become affected

early and be associated only with palatal paralysis. But as a rule this variety of paralysis occurs somewhat late, and I have seen it most often appear in the fifth, sixth, and seventh weeks of the illness. It is fortunately very short lived and has often entirely disappeared within ten days.

Paralysis of the respiratory muscles. The most fatal of all forms of paralysis, unless we include heart failure, is paralysis of the muscles of respiration. It is not very common, but, when there is generalized paralysis, it occurs with comparative frequency. Either the diaphragm or the intercostals may be affected. Usually it is the *diaphragm*, in which case breathing is carried on by the intercostals and the extraordinary muscles of respiration. As the result of this the thoracic movements are exaggerated, the lower part of the chest particularly showing expansion laterally. The abdomen, instead of being pushed out on inspiration, recedes, or it may remain apparently without motion. Mucus collects in large quantities in the air-passages, and the breathing is obviously very laboured. The condition is not always fatal, and, if the patient can be kept alive for a few days, passes off rapidly, seldom lasting more than a week. If the *intercostals* alone are paralysed, the thorax shows no expansion on inspiration, but remains almost immobile. The abdominal movements, on the other hand, are exaggerated. In my series of 915 cases, 44 showed respiratory paralysis, and in most of those many other muscles were involved. In three the diaphragm only suffered, and in about a dozen the palate was the only other muscle affected. In these last the paralysis occurred early, within three weeks of the onset. In many of the others, however, the respiratory symptoms did not appear till the fifth week and later. In only four cases of the 915 did I satisfy myself that the intercostal muscles were paralysed. In all these the paralysis involved several other muscles.

Muscles of the neck and trunk. Occasionally paralysis of the muscles of the neck and back, often of the erector spinæ group, occurs. Sixteen instances of this are included in my series, and in two of these no signs of paralysis were noted in other situations. The patient cannot turn his head in bed, or may be unable to lift it from the pillow. If he is put in a sitting position he cannot remain erect, but falls to one side. If held, his head literally wobbles on his shoulders, falling backwards, forwards, or to the side, as the case may be. I am unable to say how early this variety of muscular weakness may appear, but I do not recollect noticing it before the fifth week of illness.

Muscles of the upper extremity. The arms are rarely affected by post-diphtheritic paralysis, and only ten cases occurred in my series. The same abolition of reflexes, paræsthesia, and sensations of tingling or numbness, which are noticed in paralysis of the legs, are usually observed. The loss

of power is usually only partial, but attempts at co-ordinated movement are apt to fail, and there is often much tremor of the hand and arm when the patient wishes to grasp anything. The paralysis appears late, usually much later than that of the lower extremities, is unusual before the sixth or seventh week, and may not manifest itself till the tenth or even afterwards.

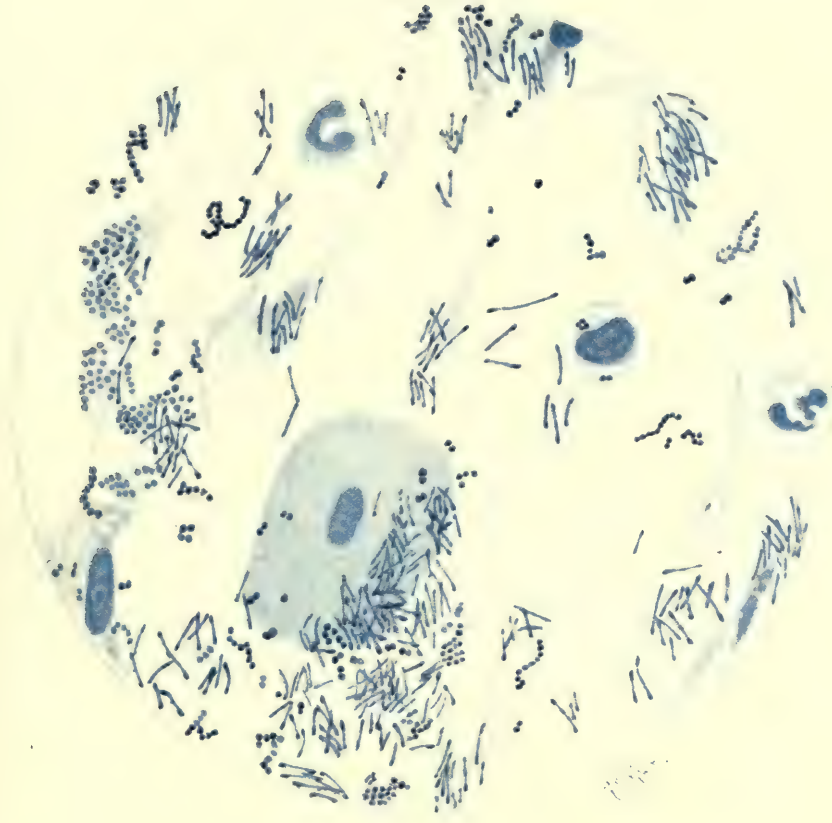
Facial paralysis. This is also relatively rare. Twenty-one cases occurred in my series, and in two of these the paralysis was limited to the facial muscles. The patient's face becomes expressionless and immobile, and, while quite alert mentally, he may look idiotic. The lips may be pendant. He is unable to whistle, or to puff out his cheeks. I have seen this condition chiefly in the later weeks of convalescence. Both sides of the face usually seem to be affected, but in two or three instances the paralysis was unilateral.

Paralysis of the levator palpebræ superioris. Ten cases of this variety of paralysis were noted in the series. In one it was the only lesion noticed. The others were associated with other forms of paralysis. The only symptom was ptosis.

Paralysis of the muscles of the larynx. Either the adductors or abductors of the larynx may become paralysed. If the former, the patient suffers from aphonia. It is said to be relatively common, and Woollacott noted it forty-eight times in a series of 478 cases of paralysis. Hoarseness and aphonia are frequently seen for some weeks after cases treated by intubation, and I have hesitated to class that form of adductor weakness as a true paralysis. Again, in severe generalized paralysis it is difficult to satisfy oneself that the adductors are involved, the pharyngeal paralysis modifying the voice and cough to a considerable extent. Ten cases, however, of paralysis of the abductors are included in my series. The symptoms in these were stridorous breathing and well-marked dyspnoea.

Paralysis of the sphincters. In severe cases of generalized paralysis, when the patient is extremely prostrated, the motions may be passed beneath him, and yet there may be but little reason to believe that any paralysis exists. True sphincter paralysis is perhaps the rarest of all the post-diphtheritic palsies. I have only seen three cases, which occurred in the series reported, and in which both bladder and rectum were involved, to the acute distress of the patients.

It will be seen, then, that almost any nerve is liable to suffer from the action of the diphtheritic toxins, and that sometimes many situations may be affected at the same moment. It is fortunate, however, that, as a rule, the various paralyses succeed each other, one often appearing as another is commencing to improve. The most complete case in my experience was



Direct swab from throat showing Klebs-Löffler bacilli, streptococci, and staphylococci. *It is seldom, however, that direct preparations are so distinct.*

Methylene blue. $\times 1000$.

one in which the palate was first affected, and shortly afterwards the accommodation. Before recovery from these, paralysis of the lower extremities was noted, and was rapidly followed by paralysis of the pharyngeal muscles and diaphragm. Lastly, the arms and sphincters were involved. All these conditions were finally recovered from.

It may be well to remark that as regards the reaction of the affected muscles to electricity there is little information to be gained either for diagnosis or prognosis.

Although *hemiplegia* following diphtheria differs in its causation from the palsies mentioned above, it may be appropriate to mention it in this place. It is very rare, but Rolleston in 1916 collected 96 cases from the literature. I have only seen one definite example in over 10,000 cases, a small girl of nine years developing complete right-sided hemiplegia with aphasia in the sixth week of the illness, at a moment when she was already suffering from extensive post-diphtheritic paralysis. As the heart's action had been extremely embarrassed it appeared probable that embolism of a small thrombus was in this instance, as in the majority of the cases in the literature, responsible for the condition. At the end of three months she had regained considerable power in the arm and leg and was talking wonderfully well. Other causes of hemiplegia may be uræmia, which is extremely rare in diphtheria, and toxic encephalitis, and I attributed to the latter cause the symptoms of a younger child who was seized with convulsions and a very transient paralysis affecting the right side, and who also completely recovered. Rolleston believes emboli, often microscopic in size, are the usual cause. Arterial spasm due to toxic irritation may explain some cases. Extensive *occlusion of the cerebral arteries* has also been reported by Rolleston, the basilar artery being plugged with thrombus which extended into the circle of Willis, and had probably formed round a small embolus.

THE BLOOD IN DIPHTHERIA. From the onset there is a moderate leucocytosis, due chiefly to an increase of polynuclear cells. In severe cases the leucocytosis is said to persist, whereas a diminution in the number of white corpuscles is usually noted in cases which are improving. Any intercurrent complication, such as broncho-pneumonia, will, however, tend to prolong the leucocytosis. According to Andrews, a low count in a case at the height of the disease, before serum has been given, is a bad sign. There seems considerable difference of opinion as to the prognostic value of blood examination, but, after studying the literature, I am inclined to believe that the systematic examination of the blood in diphtheria is of little use.

COMPLICATIONS. These are few. We have already mentioned that true nephritis is rare, and that endocarditis, if it occurs, which is very seldom, is probably due to septic rather than diphtheritic infection. The chief conditions worth mentioning are broncho-pneumonia and otitis media.

Broncho-pneumonia. As in the other infectious diseases, this complication is a much dreaded and very fatal one. It usually is seen in cases in which the larynx has been affected. It depends in most instances on septic infection, and streptococci are probably most often responsible. Occasionally, however, we have reason to believe the process is purely diphtheritic in nature. The symptoms are an elevated and persistent temperature, accompanied by rapid breathing and some cough. Areas of dullness may or may not be present, and auscultation often tells us little, the laryngeal sounds or the noise of the respiration through an intubation tube or tracheotomy canula obscuring the physical signs. Fine crepitations, however, may sometimes be heard. If the condition is extensive, the patient soon becomes somewhat cyanosed, with livid or pale face and blue lips, even if the laryngeal obstruction has been entirely obviated by successful interference. In well-marked cases the end comes rapidly, often in two or three days; the heart, already affected by the diphtheria toxin, giving in early. Patients may, on the other hand, recover, in which case the temperature, pulse, and respirations subside slowly, the normal being reached in from ten days to three weeks.

Otitis media. In most instances of this complication the ear has probably become infected by way of the Eustachian tube. The discharge often contains only septic micro-organisms, but in some cases the bacillus of diphtheria is the only germ present. At first the discharge may be quite clear and watery, but it rapidly becomes purulent. Occasionally it is sanguineous. It may appear at almost any stage of convalescence, but the condition is hardly so persistent as is the case in scarlatina, and the ear is usually dry before the patient is otherwise ready to be dismissed. I have never seen a mastoid abscess follow diphtheria. A certain number of cases show *herpes labialis*, which, according to Rolleston, may be expected in about 4 per cent. of patients. It usually occurs early, at the time of the faucial lesion.

Adenitis affecting the cervical and submaxillary glands is not very common, but may appear at almost any time in convalescence. Occasionally the enlargement is associated with the appearance of serum phenomena and may be due to the same cause, but it is also observed independently. The glands are usually very hard and seldom suppurate.

As in most other acute infectious diseases *gangrene* of the leg has been reported and is due to embolism following heart disturbances. No case

has come under my notice, but Rolleston in 1910 collected 11 cases from the literature. A case of his own, due to popliteal embolism, recovered after amputation at the knee-joint.

RELAPSE. Slight recrudescences of the throat condition are not uncommon, but a serious relapse during convalescence is comparatively rare. Membrane again appears in the fauces and the disease is repeated. It is, however, unusual for such cases to be fatal. Both recrudescences and relapses occur most frequently about three or four weeks after the original attack. Some patched throats appearing at this period seem to be serum phenomena, and are not really diphtheritic. *Second attacks* of diphtheria are common. In my twenty-three years' experience in the Edinburgh City Hospital I have had many patients under my care more than once, and in one case both attacks were of more than average severity, although the interval between them was less than two years.

DIAGNOSIS. General considerations. As the efficacy of serum treatment largely depends on its early employment, it is of the greatest importance that no time be wasted in coming to a diagnosis. The sooner the case is recognized the greater are the chances of recovery. And, as bacteriological diagnosis takes a certain amount of time, it is very desirable that a provisional conclusion be arrived at on purely clinical grounds.

Many failures to recognize a case as one of diphtheria undoubtedly depend upon neglect of the simple precaution of examining the throat. It must be remembered that many patients suffer little or no discomfort or pain in the throat, and in young children particularly we cannot expect that our attention will be drawn directly to the site of the mischief. Yet it is in young children that the worst and most fatal cases of diphtheria occur. The moral is that no ailing child has been properly examined unless the fauces have been inspected. I have seen many lamentable results of negligence as regards this important point, a doctor sometimes being in attendance daily for a week before he considered it necessary to make an examination of the throat. In such cases it is only too often that severe laryngeal symptoms or marked glandular enlargement has to develop before diphtheria is suspected, and by that time it is too late to expect much good from serum treatment.

As regards the *inspection of the throat* it is usually convenient to complete the examination of the patient before attempting it. Young children often strongly resent the introduction of the spatula, and, once they are thoroughly frightened, examination of the heart or lungs becomes extremely difficult. The throat, then, though it should be thought of first, should be looked at last. It is a good plan to only attempt at first to see the palate and

upper part of the tonsils, and not to frighten the patient by depressing the tongue too far. Many children will allow this to be done without resisting, and it not only increases their confidence but, if there is anything visible in the upper part of the fauces, a leisurely inspection of it can be made. If nothing is visible, or when the study of the lesions in this situation is completed, the tongue can be further depressed, still very gently, and the lower part of the tonsils and the pillars of the fauces examined. Lastly, the depressor can be pushed farther back and the tongue fully depressed till the child retches, displaying the posterior pharyngeal wall and the recesses behind the tonsils and pillars, and occasionally even the tip of the epiglottis. The medical man should acquire the habit of taking in all there is to be seen at a glance. Very often, in infants especially, the back of the throat is almost at once obscured by mucus or a regurgitation of milk from the stomach, and this makes it difficult to repeat the examination satisfactorily. Once a view of the throat has been obtained, if the appearances are suspicious, a swab should always be taken for bacteriological examination. As, however, it will often be necessary to act before the result of the culture can be ascertained, we have now to consider the points which guide us in coming to a provisional, or definite, clinical diagnosis.

Clinical diagnosis. Firstly, the question of *age* is of some importance. In the adult we have to consider the possibility of many throat conditions other than diphtheria, and perhaps the distinction from various forms of follicular tonsillitis will give us most trouble. But children, who form the majority of our diphtheria patients, seldom suffer from follicular tonsillitis; in fact under seven years of age the condition is comparatively rare. Suppurative tonsillitis, moreover, is not common in the first decade of life. It really almost amounts to this, that, if we can exclude scarlatina and thrush in these young patients, any visible patching or specking of the throat must be regarded as suspicious, and in any case should be treated as diphtheria.

The *situation* of the lesion may afford us considerable assistance. Patching on the pillars of the fauces, on the uvula, or on the soft palate generally, is at least likely to be diphtheritic in nature. As regards the uvula and the arch of the palate we may, it is true, have to consider Vincent's angina, but broadly speaking, a patched uvula calls for treatment with antitoxin. A lesion confined to one tonsil is, other things being equal, more likely to be diphtheritic than not, the conditions generally mistaken for diphtheria usually affecting both sides of the throat at once and to an equal degree, whereas diphtheria—though very often bilateral, it is true—is not infrequently restricted to one side of the throat, and, even if both sides are involved,

commonly shows a more extensive lesion on one tonsil than the other. Primary patches on the buccal mucous membrane and on the hard palate can only be accepted as diphtheria after some hesitation. These situations, common in thrush, are rare in diphtheria. The presence of even a most unlikely looking speck on the fauces, if any laryngeal symptoms are also present, must always be regarded as diphtheria, and immediately treated as such. Even if the diagnosis is not confirmed bacteriologically, no harm will have been done by prompt treatment, and much time will have been saved should the culture be positive. Rhinorrhœa, provided that scarlatina can be excluded, taken in conjunction with doubtful patching of the fauces, should always arouse suspicion.

As regards the *appearance* of the membranous patch it is more difficult to lay down definite rules. We have already seen that there may be great differences in the colour of true diphtheritic membrane. Still it must be admitted that a pearly grey appearance is always suspicious, although the disease cannot be excluded because a membrane is dead white or even almost bright yellow in colour. Marked lesions, with an absence of swelling or general redness, are suggestive of diphtheria, as any deep injection in a pure case of that disease is usually limited to the neighbourhood of the edges of the patch. Septic cases of diphtheria, on the other hand, present considerable inflammation, and the disease cannot therefore be excluded on that account. An important point is to decide whether the suspected patch wipes off easily or not, when firmly swabbed with a plédget of cotton-wool. If it does so, as so often happens in scarlatina throats, we can usually exclude the more serious disease with confidence. It must nevertheless be recollected that, even in untreated cases, the moment arrives when the membrane separates naturally, and that in such cases the loosening pellicle may be detached without difficulty. But in that event the separated membrane is likely to be found on the swab and can be examined at leisure. Earlier in the illness it is difficult to wipe off, or even to tear off with forceps, true diphtheritic membrane, and, should a small piece be successfully removed, it is apt to leave a bleeding surface behind it, owing to its intimate connexion with the subjacent mucous membrane. This slight hæmorrhage, however, has a greater positive than negative value in diagnosis, for bacteriology has proved that many cases in which a friable caseous deposit can be removed without much difficulty are in reality instances of true diphtheria.

As regards other considerations, a patched throat with a normal or subacute temperature should be regarded with suspicion. Many of the worst cases of diphtheria have little or no *pyrexia* and, on the other hand,

ordinary throat inflammations are accompanied as a rule by considerable fever. An absence of pain on swallowing is another suspicious feature. In diphtheria *pain* is a much less marked symptom than it is for instance in follicular tonsillitis or scarlatina, and great oedema is so comparatively rare that it is unusual for a patient to have much difficulty in opening the mouth. The presence of *albuminuria*, especially if the temperature is not high enough to suggest the probability of it being merely febrile, is a very strong point in favour of diphtheria.

Differential diagnosis of faucial diphtheria. Perhaps the greatest difficulty is to distinguish the disease from *follicular tonsillitis*. We have already noted the difference in the age incidence of the two conditions. In an ordinary case of this form of tonsillitis the distended follicles stand out as yellow points, spotted over a red background. Occasionally, however, exudation spreads from the follicles, and thus in certain places there is a suggestion of definite patching of the tonsil. In such cases the exudation wipes off readily, but it is nevertheless practically impossible to distinguish them with certainty from those diphtheritic throats in which the membrane appears to take its origin from individual tonsillar crypts. We must be largely guided by the circumstances of the case, whether, for instance, diphtheria is epidemic or not, or whether there is a history of exposure. Glandular enlargement is usually regarded as being in favour of diphtheria, but if the tonsillitis is septic in origin the glands are equally likely to be affected. Albuminuria is a point of more importance. In a doubtful case, when there is no particular reason to believe it is diphtheria and the lesions are limited to quite discrete specks, it is safe to take a culture only and wait for twenty-four hours, by which time, if the disease is really diphtheria, the separate patches will have merged into a uniform pellicle. If there is a history of exposure serum should be given without waiting.

As a rule there is little trouble in diagnosing diphtheria from *quinsy*. Suppuration of the tonsil in diphtheria is most unusual, and if, therefore, one of the tonsils is so much enlarged as to give a quite asymmetrical appearance to the back of the throat, or if there is much protrusion downwards of the soft palate on the affected side, we need not as a rule suspect diphtheria even if some suggestion of exudation be present. After a tonsillar abscess has been incised, however, the sloughy grey appearance of the neighbourhood of the wound often simulates a diphtheritic membrane. There is no tendency in such cases for the tonsil to be involved in this process except near the edges of the wound, and failure of an apparent membrane to show any signs of spreading within twenty-four hours should sufficiently clear up the case. In some cases of quinsy the abscess ruptures

at some point high up and at the back of the tonsil, and from this opening, usually minute, a thin film of purulent matter spreads over the surface of the gland, a little more pus being squeezed out with each attempt at swallowing. In this way an ugly-looking coating of pus and sticky débris gradually collects on the tonsil, and, as it is often difficult to obtain a satisfactory view of the condition, owing to the patient being unable to open the mouth properly, it is not surprising that such cases are sometimes notified as diphtheria. The apparent membrane, however, in these patients wipes off quite easily, and if a satisfactory view of the throat can be obtained the mistake should not be made. I am bound to admit, nevertheless, that a vague glimpse of a coated tonsil, through jaws almost entirely closed, has occasionally made me feel that it is advisable to give the patient the benefit of the doubt, that is to say, an injection of serum, although in my experience it is most unusual for a patient who cannot open his mouth to turn out to be a genuine case of diphtheria. It may be added that quinsy is often accompanied by well-marked fever, the temperature frequently being as high as 104°, and not rarely is febrile albuminuria also present.

We may also experience difficulty with various *ulcerated throats*. Diphtheria does not of itself cause any real loss of tissue, but it is wonderful how difficult it is in some lights to distinguish a shallow excavated ulcer with a sloughing base from an actual surface exudation. We meet these ulcerations in various forms of septic sore throat and also in septic scarlatina. They are usually situated on the tonsils and may be accompanied by considerable glandular enlargement and high fever. *Syphilitic ulcerations* must also be remembered. Occasionally their appearance very closely resembles that of diphtheria, and attempts to remove the sloughing surface often cause a little hæmorrhage. The temperature, moreover, may be normal, and if the suspected patch is far back and not easily seen it is not unusual for a mistake to be made. Fortunately syphilitic lesions are usually situated well forward in the throat, sometimes even on the hard palate. I have seen the uvula and arch covered with a slough which exactly resembles diphtheritic membrane, and which, after several negative cultures and an entirely ineffective employment of serum, yielded to mercury and iodide. Usually, however, the slough will be seen to be depressed and the edges of the ulceration more or less clearly defined. A history of syphilis, if obtainable, is of much assistance in coming to a conclusion. Such lesions may be either late secondary, or tertiary, in their character. *Tubercular ulceration*, again, is sometimes mistaken for diphtheria. Its chronicity and the presence of tubercular lesions elsewhere should make its recognition not too difficult.

Thrush should always be thought of in young children, and also in adults in the last stages of exhausting diseases such as phthisis. The patches are usually milk white in colour. They occur in almost any situation and are not infrequently noticed on the palate. The tongue and lips are also often affected. There is practically no surrounding inflammation, and the pellicle swabs off easily, leaving a normal-looking mucous membrane behind it. Microscopic examination reveals mycelia and spores.

Herpes occasionally affects the fauces. Even in this situation it should not be difficult to recognize. The vesicles, often broken, and presenting a white base with a red areola, lie quite separate from each other. Occasionally the diagnosis is much assisted by the presence of crops of herpes on the lips or skin. It must not be forgotten, nevertheless, that in some outbreaks of diphtheria herpes is not very rare, and that therefore the mere presence of vesicles on the lips cannot be taken as contradicting a diagnosis of diphtheria in the fauces.

The action of caustics may cause appearances not unlike that of a diphtheritic membrane. Carbolic acid, strong alkalies, and powerful antiseptics employed therapeutically, leave the surface of the mucous membrane grey or white in colour, and occasionally the whole affected area sloughs. Scalding of the throat from steam or hot water has the same effects. Much difficulty, however, is not likely to arise in diagnosis except in those cases where too strong an antiseptic preparation has been employed, and even then, if a good view of the throat can be obtained, it is not probable that a mistake will be made.

As regards all these patched and spotted throats, the concurrent appearance of croup, the presence of albuminuria, and the subsequent development of paralysis are arguments in favour of a diagnosis of diphtheria.

Apart from the above conditions, our chief difficulty will be the differentiation of diphtheria from *scarlatina*. This question is much complicated by the comparative frequency with which we find the two diseases coexisting in the same patient. A case, then, may be one of diphtheria, of scarlatina, or of both together. Not much is to be gathered from the history of the initial symptoms. It is true vomiting is a much more common symptom in scarlatina than it is in diphtheria, but, on the other hand, in some diphtheria outbreaks nearly all patients vomit. The rash of scarlatina, if well developed, will at least prove the presence of that disease, but it must be remembered that erythematous rashes are occasionally met with in diphtheria and may resemble that of scarlatina sufficiently to cause trouble, although usually they present differences in their distribution over the body, being scarcely so general. But the absence of a rash often

helps us little, as, if the case is not seen till the third or fourth day, any eruption may have altogether disappeared. For instance, in hospital practice a case is often notified as diphtheria on the strength of a severely patched throat. The rash has disappeared, the desquamation has not begun, and on admission the condition may be quite unrecognizable. In these patients we may often gain great assistance from the study of the tongue. The brilliant red strawberry tongue of scarlatina should be visible in a case of that disease from the fourth to the sixth day, and its presence at such a date in a doubtful case should lead us to a diagnosis of scarlatina. The earlier tongue of the 'white strawberry' type is of much less value, and is, indeed, frequently seen in uncomplicated diphtheria. A patient whose tongue has not desquamated, leaving a raw denuded surface studded with œdematous papillæ, by the fifth or sixth day of his illness is most unlikely to be suffering from scarlet fever.

I am inclined to believe that the septic type of scarlatina, which is accompanied by throats liable to be mistaken for diphtheria, is characterized by a flushed rather than by a pale face, whereas a patient suffering from well-marked diphtheria will be probably pale by the fourth or fifth day of his illness, even if he has previously presented a complexion resembling that of scarlatina. The scarlatina patient, moreover, is much more likely to be irritable and restless than is the sufferer from diphtheria at this time of the disease.

As regards the throat itself, the angry redness usually observed in scarlet fever is generally distributed over the whole of the fauces, including the soft palate, which in the early stage presents a punctate spotting. In diphtheria the throat may also be red, but the colour is seldom of the same deep tint, and is more likely to be best marked round the lesions. The palate is often quite pale unless there is actually membrane upon it, in which event the case is practically certain to be one of diphtheria, whether in conjunction with scarlatina or not. As to the patches, those seen in the early stage of scarlatina, while sometimes bearing a strong resemblance to diphtheritic membrane, are in reality composed of soft pultaceous material which wipes off easily and does not leave a bleeding surface behind it. Later in the disease superficial sloughs of the tonsils may be seen, and there is often a tendency to ulceration, with sometimes a considerable loss of tissue, and, in a bad case, actual gangrene. Rhinorrhœa is met with in both diseases and therefore its presence is of no assistance to us. Glands are more likely to be very much enlarged in scarlatina, but as the glandular enlargement in septic cases of diphtheria may be excessive, and, on the other hand, the adenitis may be comparatively slight in both diseases, we

cannot obtain much help from this source. Albuminuria may occur in traces in early scarlatina with high fever, but usually is postponed till convalescence. In diphtheria it is a comparatively early symptom and, if the fever is moderate, gives great help in diagnosis. Many cases will be impossible to diagnose with certainty and will require to be watched for some days, when the appearance of characteristic pin-hole desquamation, early arthritis, or nephritis in the third week of the illness will settle the question in favour of scarlatina. Bacteriological diagnosis will decide if diphtheria is also present or not, and, again, the usual sequelæ of that disease may assist us.

It should be unnecessary to mention *mumps*, for which in my experience, however, diphtheria with great glandular enlargement is far too often mistaken, especially if the former disease is epidemic. I have seen many lives lost from the omission of the simple precaution of examining the throat; so many, indeed, that I am inclined to regard sceptically many of the paralytic complications attributed to mumps and which have often a suspicious resemblance to post-diphtheritic phenomena.

In coming to a diagnosis it is well to remember the existence of the condition known as **Vincent's angina**. This is an infective inflammation of the throat, accompanied by the formation of a pseudo-membranous slough, which, in the cases I have personally observed, has been usually somewhat gelatinous in appearance, and greenish grey in colour. The patch is most difficult to remove, and is often situated on the upper part of the tonsil, the anterior pillar, or the free edge of the arch of the palate. The uvula is sometimes affected. On removal, an ulcerated surface is left which is said to bleed freely, but certainly does not always do so. The condition may be accompanied by an ulcerative stomatitis which is believed to depend on the same micro-organism, a fusiform bacillus, found usually in association with a motile spirillum (see Plate XXIII). I have found it most difficult to recognize this condition on purely clinical evidence. Sometimes it very closely resembles diphtheria. Should no diphtheria bacilli be present in the smears or cultures from a suggestive throat, the organisms of Vincent should always be looked for. A patient suffering from this condition usually has some fever and adenitis. Occasionally Vincent's angina occurs in epidemic form, and it may be found in association with true diphtheria itself. Under such circumstances the persistence of the local lesion, in spite of appropriate serum treatment, should arouse suspicion.

Stomatitis, due to the organisms of Vincent, has been fairly common among our troops during the war, and the most frequently observed lesion has been extensive ulceration of the gums, at the roots of the teeth, with purulent discharge. Many of these cases, which have developed subse-

PLATE XXIII.

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Direct swab from throat showing the bacilli and spirilla of Vincent's angina.

Leishman's stain. × 1000.

quently suspicious patches of ulceration on the fauces, have been sent into hospital as diphtheria, and I have found the associated inflammation of the gums of the greatest aid in making a distinction. It may be mentioned that the ulceration in septic cases of scarlet fever is probably often due to the Vincent organisms. We may add that painting with tincture of iodine appears to give fairly satisfactory results in treatment.

Differential diagnosis of laryngeal diphtheria. The occurrence of symptoms of croup in a young child should always arouse a suspicion of diphtheria, and unless there is direct evidence to the contrary the case should be treated with serum at once. As has been said above, the co-existence of laryngeal symptoms with even a small amount of unlikely looking exudation on the fauces may be taken for practical purposes as a proof of diphtheria. It will be remembered that laryngitis is an extremely rare symptom in scarlatina, so that disease can be at once excluded. In hospital practice our chief difficulty is probably the differentiation of diphtheritic croup from the laryngitis which so frequently precedes *measles*. It is a sound rule to isolate every croupy patient who does not present on admission distinct patching on the fauces. This point is alluded to in the chapter on Measles. Suffice it to say here that Koplik's spots and stomatitis should always be looked for, and due weight given to such symptoms as sneezing and lachrymation. It may be noted that a similar laryngitis, sometimes actually obstructive, occasionally occurs in the catarrhal stage of *whooping-cough*.

As regards *simple laryngitis* the distinction may be a matter of great difficulty. Some children suffer from recurrent attacks of croup which occasionally may assume a serious aspect. These attacks usually appear suddenly at night, and between them the patient is often to all appearance quite well. A history of such paroxysms on previous occasions would make us doubt the existence of the more severe condition. In such cases, short of a history of actual exposure to infection, it may be permissible to await the result of a culture and trust to palliative measures, but if the dyspnœa is well marked and persistent it is wiser to give the patient the benefit of the doubt and inject antitoxin. Another condition not infrequently notified as diphtheria is *Laryngismus Stridulus*. This is, however, only found in very young children, seldom if ever in patients over two years of age, and, as it is regarded as one of the manifestations of rickets, we would expect that some evidence of that disease will be present. The outstanding symptom of laryngismus is a more or less prolonged period of apnœa, due to spasm, followed by loud crowing gasps as the spasm relaxes. The attacks may be frequently repeated during the night, but between them the patient is, as a rule, fairly comfortable. The convulsive character of the affection

is sometimes evidenced by a condition resembling tetany accompanying the laryngeal spasm. Strabismus and actual convulsions may also be observed. Any symptoms of this nature help to indicate the true nature of a doubtful case. *Paralysis* of the abductor muscles of the larynx may be responsible for a dyspnœa which has been mistaken for diphtheria. In adults this is due to nervous diseases, in children the most likely cause is post-diphtheritic paralysis, of which, no doubt, other indications will be present. *Œdema of the glottis* is another condition which is chiefly seen in adults and the nature of which may be recognized by a study of the general circumstances of the case. In patients whose dyspnœa has appeared very suddenly it may be worth while considering the possibility of a *foreign body* in the larynx.

The pressure of an *enlarged thymus gland* occasionally causes considerable obstruction or even rapid death from acute dyspnœa. In two cases in my experience an unnaturally large thymus was the only cause found post mortem to which death could, with any reason, be attributed, and I have suspected the existence of this condition in two or three patients who survived, and whose persistent dyspnœa was otherwise quite unexplained. All these patients were infants of under a year. D'Oelsnitz states that the condition is characterized by the fact that recession is more marked when the patient is recumbent, that the chest is flattened laterally with projection of the sternum, and that pressure with the finger from above on the thymus at the supra-sternal notch causes the recession to temporarily disappear.

The possibility of a *retro-pharyngeal abscess* must also be remembered. It is a good rule, when no other cause can be found for severe dyspnœa, to examine the posterior wall of the pharynx with the finger, in which case fluctuation, if present, is readily recognized. In one or two cases, admitted apparently moribund and demanding instant operative interference, I have discovered the presence of the abscess in the act of intubating the larynx. We would expect to find a history of a fairly gradual onset of dyspnœa, prolonged indeed over several days, but in some patients the severe symptoms seem to appear with great rapidity. The patient usually holds the head somewhat retracted, a position which, no doubt, allows a better entrance for the air, and there may be considerable cervical swelling, which is hardly likely to be found in a case of diphtheria in which the lesions are entirely confined to the larynx.

THE BACTERIOLOGICAL DIAGNOSIS OF DIPHTHERIA. It has perhaps been already sufficiently emphasized that the first duty of the practitioner is to treat a doubtful case, after which he is at liberty to diagnose

it. There is often far too much valuable time wasted in awaiting the report from a bacteriological laboratory. But we must nevertheless thoroughly appreciate the fact that bacteriology remains the final court of appeal if we desire to know the true nature of a case. It has, no doubt, its limitations, but its systematic application to all suspected cases is of the utmost value from the point of view of public health. On the other hand, it is a fatal mistake to put any stress on one or two negative reports. Usually the case which is suspicious enough to examine bacteriologically is also suspicious enough to treat with serum.

But waiting is not always a necessity even for reliable bacteriological information. The direct examination of a *smear preparation* can be made in a few minutes, and often gives the most trustworthy results. We find, indeed, that in 75 per cent. at least of our cases the result of the direct smear preparation is verified by the result of the subsequent cultures. All that is required is a microscope fitted with an oil immersion lens and a few staining reagents, and any practitioner can make the diagnosis for himself. It is surprising that a method of diagnosis so completely reliable is so little employed. Its use, moreover, has the further advantage of giving some indication of the association of various organisms in the throat, a point which may be of importance in prognosis. And on several occasions in my experience the detection of spirilla or of fusiform bacilli in the smear preparation has first directed our attention to the possibility of the case being one of Vincent's angina, a condition which might never have been detected had cultures alone been depended on.

Even a simple stain such as gentian violet is of value in preparing a smear. The presence of slender rods, characteristically grouped in masses, or scattered through the field, and showing here and there V-shaped arrangements, is sufficient justification for giving antitoxic serum. Still better is Löffler's methylene blue, a stain which not only shows very well the general arrangement of the organisms, but also brings out their segmented appearance. A more delicate stain, and one which at the Edinburgh City Hospital is used as a routine, is toluidin blue.¹ The dried film is stained from twenty-five to thirty seconds, and the stain may be blotted off, or the preparation very lightly and quickly washed. Care must be taken not to overstain. The bodies of the bacilli are very faintly coloured, while the polar staining is exceedingly well marked and characteristic. Toluidin Blue is hardly

¹ Toluidin blue	0.05 gramme
Absolute alcohol	1.0 c.c.
Glacial acetic acid	2.5 c.c.
Distilled water	50.0 c.c.

so satisfactory as Löffler's if a general view of the smear is desired. Careful focusing is necessary and the results of overstaining more disastrous. But after some practice it will probably be found the most reliable stain for the identification of the bacillus in a smear preparation. Artificial light is required and the higher the magnification the better (see Plate XXIV).

The smear itself may be made by rubbing a sterilized cotton-wool swab, which has been firmly applied to the affected parts of the throat, on the surface of a cover slip or glass slide. If actual pieces of membrane adhere to the swab, they may be picked off, washed in tap water to remove superficial contaminations, and teased out on the slide. The swab may then be used for making a culture. If dry, a little normal saline may be dropped upon it.

The best medium for *cultures* is Löffler's blood serum, upon which, after incubation at body temperature for about twelve hours, the small round whitish colonies may be readily recognized. For examining the cultures microscopically the most reliable stain is Neisser's Acid Methylene Blue.¹ As a counterstain, instead of the Bismarck Brown which was originally recommended, Picro-Erythrosin² will be found to give very beautiful results, the protoplasm of the bacilli being stained a pale pink and the granules almost black in colour. The film is stained first with the blue for from one to three seconds and washed very lightly and rapidly, the counterstain being used for about the same time and then blotted or washed off (see Plate XX).

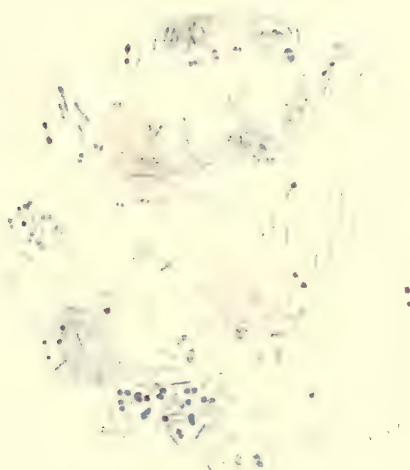
The presence of rod-shaped organisms, either long or short, showing marked beading, may be taken for all practical purposes as a proof of diphtheria. It is, of course, the case that under certain circumstances true diphtheria bacilli may stain evenly throughout, but these forms are comparatively rarely met with, at least in young cultures, and in any case their differentiation from Hofmann's bacillus must be left to skilled bacteriologists. Indeed, when it is remembered that a volume as large as this has been devoted to the bacteriology of diphtheria alone, it cannot reasonably be expected that the general practitioner will attempt to do more than rely upon some easily worked test, and in Neisser's stain he has at his hand one which is sufficiently reliable. The bacillus of Hofmann (see Plate XX)

¹ Acid Methylene Blue	0.1 gramme
Alcohol	2.0 c.c.
Glacial Acetic Acid	5.0 c.c.
Distilled Water	95.0 c.c.

² Equal parts of a 1 per cent. aqueous solution of picric acid and of a 1 per cent. aqueous solution of erythrosin. Enough lithium carbonate to cover the bottom of the bottle is required to keep the mixture in solution.

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PLATE XXIV.



Direct swab from Diphtheria showing polar stained rods, which may be regarded as diagnostic.

Toluidin blue. × 1000.

is met in many throats, and its relation to the diphtheria bacillus has been the subject of much controversy. It is a short rod, and, both in the smear and the culture, usually assumes a different arrangement from the Löffler bacillus, tending to lie in parallel lines. It stains evenly, shows no beading, and occasionally has an unstained septum across its centre. It grows well on the ordinary media which suit the diphtheria bacillus, but its colonies are more opaque, and, unlike the other micro-organism, it does not cause acid formation in a glucose medium. It is not pathogenic to guinea-pigs, and it is a debated point whether it is, or is not, responsible for any pathological throat conditions.

The final test is the subcutaneous injection of the suspected organism into small animals. This adds considerably to the time which may have already been wasted in waiting for the result of a culture. The test must be performed by a competent bacteriologist. As the result of inoculation with a virulent organism a guinea-pig dies in less than thirty-six hours. Occasionally, however, a true diphtheria bacillus may be non-virulent, and therefore even this physiological test is not entirely satisfactory.

Deductions to be drawn from the different methods of bacteriological diagnosis. It has already been stated that in a well-marked case of sore throat, which is suspicious enough to make bacteriological examination desirable, it is a good rule to inject serum first and inquire into the causative organism afterwards. In any case a negative result from a culture must be disregarded. Even from severe throats of typical diphtheria cases I have seen the cultures repeatedly negative for three or four days, in some patients indeed persistently negative throughout the illness even when characteristic paralysis has followed. It would be therefore most unsafe to regard a negative finding as absolute. On the other hand, if the result is positive, it may be assumed for all practical purposes that the throat condition is diphtheria. Even here there is a slight element of uncertainty. Some persons harbour the diphtheria bacillus for long periods in a perfectly healthy throat, and it is conceivable that they might suffer from a simple tonsillitis quite independently of the presence of the bacillus. In such cases, nevertheless, it is reasonable to assume that the probabilities of true diphtheria ensuing are enormous, and therefore it is always good practice to give serum, if only as a prophylactic.

In cases of very slight sore throat, when the bacteriological examination is made as a purely precautionary measure, the direct smear examination will be found especially useful. If it is negative it is quite justifiable to await the result of the culture before thinking it necessary to administer antitoxin. In more severe throats, even in the face of a negative smear

examination, it is always safer to give a moderate dose of serum, if only 3,000 or 4,000 units.

In conclusion it may be said that while the confirmatory evidence of a positive culture is most valuable, particularly from the public health point of view, it is wise not to put too much reliance on bacteriology, and never to be guided by it if it is opposed by clinical evidence. I think that those physicians who have much experience of diphtheria are in the habit, when they come across a suspicious case, of giving it what we call in Scotland 'Jeddart justice', which consists in hanging a suspected person first and trying him afterwards.

PROGNOSIS. The chances of recovery of a diphtheria patient have so much improved during recent years owing to the introduction of serum treatment that we have to go back to the pre-antitoxin days to ascertain what may be fairly considered as the natural *mortality* of the disease. At that period the Edinburgh Hospital death-rate was from 25 to 30 per cent., and this must be regarded as a very moderate figure. The Metropolitan Asylums Board statistics show that in the last five years prior to the introduction of antitoxin the mortality from diphtheria in their hospitals was about 33 per cent. Rosenthal, who collected from various sources records of 183,256 cases, states that the death-rate all over averaged over 38 per cent. It must, of course, be frankly admitted that bacteriological diagnosis, and the consequent inclusion of larger numbers of mild cases in more modern statistics, has done something to lower the percentage mortality, but, nevertheless, even under the present conditions, it would be reasonable to expect a death-rate of from 20 to 25 per cent. in cases not treated with serum. For serum-treated cases, from 3 to 14 per cent., according to the virulence of the epidemic, would be a fair figure.

We will first, then, be influenced in our prognosis by the question of *treatment*. If serum is available, the patient's chances are enormously improved. Further, the earlier serum treatment is started the better are the results obtained. It is extremely rare for a patient injected on the first day of illness to succumb, and my experience has been that of cases treated within forty-eight hours of the onset of the disease the death-rate seldom exceeds 3 per cent., and may be very much less. It rises, however, with each succeeding day, and for cases injected for the first time after a week has elapsed it not infrequently is above 20 per cent. (see Table E, p. 435). Paralysis, moreover, is liable to be more frequent in cases which receive serum late. (Table F, p. 436.)

Apart altogether from serum treatment, however, the general management of the patient influences the prognosis. The mildest case of diphtheria

may become serious if care is not taken and the patient is not confined to bed. In hospitals it is extremely rare to see a case with trivial faucial lesions terminate fatally or develop dangerous sequelæ, and this, in my opinion, may be largely attributed to the fact that even the mildest cases are usually kept in the recumbent posture for at least three weeks. On the other hand, if the patient is allowed to rise too early, or to exert himself unduly, cardiac failure or various forms of paralysis may supervene. Paralysis particularly is much more likely to occur if the muscles liable to be affected have been too much exercised.

Next, the *situation of the lesions* must be considered. If the larynx is implicated the mortality is always considerably higher than the general average for all cases. Even in mild outbreaks the death-rate in Edinburgh has never been lower than 11 per cent. and recently has averaged from 20 to 25 per cent. If, however, a patient survives the laryngeal obstruction, his chances of ultimate recovery are good, always provided his faucial lesions have not been severe. This favourable outlook is due to the rarity of heart failure and paralysis in purely laryngeal cases. The most fatal lesions are those which involve the nasal cavities when the fauces are also affected. The death-rate of these naso-pharyngeal cases still remains from 25 to 40 per cent., and it is particularly in such patients that heart failure is to be dreaded and the various forms of paralysis confidently expected. In faucial diphtheria the chances of recovery are good, provided the lesions are limited to the tonsils. If, however, the uvula, the pillars of the fauces, or the palate are involved, the probability of severe sequelæ, or of a fatal termination, is considerably increased. As regards other situations, it may be added that diphtheria affecting the vulva must always be regarded as dangerous.

As regards *type* severe toxic and septic cases are most liable to cardiac failure, even if the throat and general symptoms clear up satisfactorily. True hæmorrhagic cases—that is to say, cases in which definite hæmorrhages, not unlike blots of ink, have occurred into the skin—are, in my experience at least, invariably fatal. On the other hand, patients who, in addition to severe symptoms, have manifested a hæmorrhagic tendency, as evidenced by epistaxis and marked bruising at the site of injection, may occasionally recover.

Much may be learned from the *appearance* of the patient. Some present a livid or waxy pale complexion, and an expression which can only be described as 'poisoned', and it is rare to see such patients recover. Very marked glandular enlargement is usually a bad sign, particularly if the glands meet round the neck in a 'collar'. Early albuminuria, drowsiness, and

either a very rapid or a very slow pulse are signs of evil import. In most cases of well-marked diphtheria there is a distinctly foul odour from the throat. If this is particularly putrid, it usually marks an especially bad case. As regards the *temperature*, it is well to remember that its return to normal in no way indicates any improvement in the course of the case. On the contrary, it is often merely a sign of the prostration of the patient and of a bad reaction on his part to the infection. A severely patched throat with a normal or subnormal temperature is no cause for gratification (see Fig. 48). The average fatal case terminates with the temperature subnormal. In mild favourable cases, on the other hand, the subsidence of the pyrexia may be regarded as a step towards recovery, and so far is, no doubt, satisfactory. Much the same may be said of the temperature in laryngeal diphtheria, in which a return to normal is welcomed as indicating that there is no broncho-pneumonia, that much dreaded complication being usually accompanied by considerable fever of an irregular type. In children who have been intubated, moreover, I have found that the chances of the patient finally dispensing with the tube are much greater after the temperature has fallen.

It must never be forgotten that the *age* of the patient is of great importance in prognosis. Very young children have a very high mortality, especially if the disease assumes the laryngeal form. Patients of under ten years of age appear to suffer much more severely than adolescents and young adults, in whom, for the most part, the chances of recovery are exceedingly favourable. In older people, on the other hand, and especially in the aged, the disease is apt to prove more fatal. Although the infection is more common in females than males after the age of ten, prognosis is not to any extent influenced by the *sex* of the patient.

To turn from the general considerations discussed above to the question of prognosis as affected by various circumstances occurring in the course of the case, it may be said that the *pulse* must always be most carefully watched. Irregularity, either in strength or in rhythm, and intermission should always cause anxiety. If, in addition to this, there is any tendency to coldness of the extremities the outlook is especially grave. We have already seen that progressive increase in the liver dullness sometimes precedes cardiac failure. A sudden change in the rate of the pulse, from fifteen to twenty beats, whether the change is in the direction of an increased or a decreased rate, is in my experience of most evil omen, being often followed by all the signs of cardiac failure. It is highly important therefore to have the pulse counted at least every four hours, and to make the nurse in charge understand that any sudden change in its rapidity

should be at once reported. Signs of cardiac dilatation, feebleness of the first sound, and gallop rhythm should cause anxiety, especially the last, although I have seen a fair number of recoveries in the patients who manifested it. Definite enlargement of the liver is also a serious symptom. A very serious symptom is *vomiting*, which often precedes cardiac failure. It is obvious that the child who is convalescent from diphtheria may vomit from all sorts of causes, although, if proper care is taken with the feeding, such attacks are relatively rare. But in probably more than half the patients who vomit during the course of the disease this symptom is the herald of grave cardiac complications. Even granting that the cause of the symptom is not always cardiac, we all know the great strain caused by a bad attack of vomiting, and I have seen on two or three occasions alarming cardiac weakness follow paroxysms of vomiting which were unquestionably due to indiscretions of diet. Therefore, whether we regard the vomiting as a symptom of an already existing cardiac failure, or as the possible cause of a subsequent failure, it may well give reason for alarm, and the patient requires our services at once. A patient with a failing heart who suffers from vomiting very seldom recovers. Præcordial or referred pain is an even more fatal sign, as is also the restlessness so common in cardiac cases. We have already noted that albuminuria occurring in the first few days of the illness marks a bad case. We may add here that, if it becomes excessive in amount and if the urine is much decreased in quantity, the outlook for the patient is extremely serious.

As regards *paralysis* the prognosis is good as long as the respiratory muscles are not affected. The condition is often a tedious one, but, with the above reservation, a hopeful view may be taken, as function is practically certain to be recovered, and that usually within three months. As apart from respiratory paralysis, the most serious muscular weakness is that affecting the pharyngeal constrictors. Not only is there great danger of choking, but it is particularly this form of paralysis which is most often followed by diaphragmatic or intercostal disability.

By way of conclusion it may be said that every case of diphtheria, however insignificant, entails a certain amount of risk. This risk, however, may in mild or moderate cases be minimized, if not actually abolished, by appropriate and early treatment. Once the diagnosis has been definitely made, the local lesion can always be held in check by serum treatment, and, if an adequate dose is administered within forty-eight hours of the onset of symptoms, the chances of the ugliest looking case, provided it is not hæmorrhagic, are extremely good. There is little reason to dread the spread of infection to the larynx or nose if these situations are free

from membrane at the time of the first injection. This risk, once the most feared of all the complications of faucial diphtheria, has practically ceased to exist since antitoxin was introduced. If, however, patients when they come under observation already present laryngeal or nasal lesions, the prognosis becomes much more grave, and especially so for the nasal cases, which are responsible for the majority of deaths from cardiac failure and for the most severe examples of paralysis. The less certainty we have that any given patient will be kept a sufficient time in the recumbent posture, or that care will be taken as regards the dieting and nursing, the more guarded, even for the mildest cases, the prognosis must be.

A few words may be added on the subject of *bacteriological prognosis*. The association of the Löffler bacillus with either the streptococcus or the staphylococcus, particularly if these organisms appear to be present in very large numbers in the smear preparation, adds very much to the gravity of the case. Personally I have always regarded the staphylococcic cases as the most severe, and latterly that opinion seems to be confirmed by the experience of other observers.

TREATMENT. The treatment of diphtheria, formerly practically useless, has become since the introduction of antitoxic serum very effective, and if we were always certain of seeing our patients on the first day of their illness very few words would be needed to describe it. It would be sufficient to say that antitoxin should be at once injected and the patient kept at rest in bed for a fortnight or three weeks. But we cannot expect to be so fortunate. Patients often come comparatively late under treatment, or, again, the true nature of the condition may not at first be fully realized. And so it is that diphtheria still remains a most dangerous infection, and one which still affords many opportunities for forms of treatment other than the mere injection of serum. We will consider first, however, the questions which arise in connexion with the administration of antitoxin, as being by far the most important. Thereafter local applications, general constitutional treatment, and the management of the various conditions which complicate the disease, may with advantage be discussed.

SERUM TREATMENT. Preparation of antitoxin. The first necessity for the production of antitoxic serum is the preparation of a strong toxin. Bacilli of virulent strains are cultivated upon a suitable fluid medium, and in the process of their multiplication give off large quantities of toxin into the fluid. After growth has been permitted for about a fortnight the culture medium is passed through a porcelain filter which retains the bacilli, the filtrate being a strong solution of toxin. This is standardized by the physiological test of determining its action upon small animals. The

minimum lethal dose, or *toxic unit*, is that amount of toxin which will cause the death of a guinea-pig, weighing 250 grammes, in four days. One-tenth of a cubic centimetre of an averagely strong toxin should be sufficient for this purpose.

The animal chosen for the production of the antitoxin is the horse. Care is exercised in the selection of the horses employed, and they are proved to be free from tubercle or glanders by the tuberculin and mallein tests. At first only small doses, often not exceeding one cubic centimetre of toxin, are injected. A local reaction follows, and there is also some fever and constitutional disturbance. When these symptoms have subsided another injection is given. The doses are gradually increased, and after some months enormous quantities of toxin are well tolerated. The antitoxic power of the blood continues to increase, till about six months after the first injection it reaches its highest point. The horse can then be bled at suitable intervals, and the separated blood-serum becomes the antitoxin of commerce. A small percentage of an antiseptic is added to assist in its preservation.

The *antitoxic unit* is the smallest amount of antitoxin which will neutralize one hundred times the minimum lethal dose given to a guinea-pig of appropriate weight. The toxin and antitoxin are mixed and injected together, and the animal suffers no ill results. The adoption of the standard of the unit enables us to attain to some accuracy in dosage. Before its introduction so many cubic centimetres were injected, but there was no means of ascertaining the potency of the antitoxin, and the results obtained were most irregular. Some horses can produce a much more potent serum than others. Nowadays the serum is sold by the unit, the vials being labelled as containing 1,500 or 6,000 units, and so on, irrespective of the amount of serum. An average commercial serum contains about 500 units to the cubic centimetre, but it is often convenient to use more potent preparations, by the use of which large doses can be given in small bulk. Some serums are of the strength of 1,000 units to the cubic centimetre, and naturally these are more expensive to produce, and their cost is correspondingly higher. The antitoxin is often guaranteed to preserve its labelled strength for at least a year.

The value of antitoxin in diphtheria. Every fair-minded man will, of course, admit that all the reduction in the mortality of diphtheria, since the introduction of antitoxin, is not due to its employment. Unquestionably, bacteriological diagnosis has caused the inclusion in our statistics of a certain number of cases which, twenty-five years ago, would not have been classed as diphtheria. But when we consider the remarkably reduced death-rate of patients suffering from the laryngeal form of the disease, which was as

easy to recognize in the days before bacteriological diagnosis as it is to-day, we feel that we stand upon firm ground. An even more fixed type is represented by those laryngeal cases which are severe enough to require operative interference. The mortality of these has been reduced from over 70 per cent. to about 30 per cent., and that, not in one hospital, or even in one country, but practically all over the world and almost simultaneously. Again, all who have had experience of diphtheria, both before and since the introduction of serum treatment, must have been struck by the rarity of any marked spread of the false membrane after an injection of antitoxin, and especially of extension to the larynx. Lastly, if indeed it is necessary to add anything more, the fact that the patient's chances of recovery steadily grow less with each day that the administration of serum is postponed, as is proved by innumerable statistical tables, should be enough to convince any ordinary person that, in antitoxin, we possess a genuine specific for the treatment of diphtheria (see Table E, p. 435).

The fact that paralysis is met with more frequently at the present day than it formerly was is readily accounted for, first by the fact that a larger number of very severe cases survive long enough to manifest it, and secondly by the greater attention which has been recently directed to its slighter forms. The introduction of serum treatment has certainly produced a greater interest in what was formerly regarded as a very hopeless disease.

As regards the choice of a serum, there is little to be said. I have had excellent results, at one time or another, with most of those on the market. In the early days of the treatment some of the serums were not very good, and the effect of any given dose was often uncertain. Thanks, however, to modern standardization, we now can usually roughly estimate the size of the dose required. I say 'roughly' advisedly, because the question of dosage must remain always more or less a matter of opinion. It is impossible to gauge, with absolute accuracy, the amount of toxæmia from which any given patient may be suffering. All we can expect to do is to give such a dose as has, in our previous experience, proved satisfactory in patients who have presented corresponding lesions and whose general condition has appeared similar. I will endeavour to lay down the principles which guide me in coming to a decision as to what the dose is to be.

First, then, we require to have a clear idea of what we may fairly expect the antitoxin to accomplish. It would appear that all that can be hoped is that in addition to breaking up, and limiting the spread of, the false membrane, it will neutralize the toxin which is free in the blood at the moment of injection. It is possible also that it may detach any toxin which has only recently entered into loose combination with the tissues, but too

much must not be expected as regards this. It would appear, then, useless and wasteful to inject a much larger amount than can be taken up by the circulating toxin. What is to be the *maximum dose* at a single injection? When serum was first introduced the dosage was undoubtedly for the most part too small, and, as the doses gradually increased, it was interesting to note that the mortality proportionately decreased. For some time, however, when I began to use large doses of 16,000 to 20,000 units for a single first injection in very severe cases I did not notice any particular improvement in my results, and I have now returned to doses of 10,000 units as a rough maximum, repeating the injections at intervals of 8, 12, or 24 hours as may be required. The expense of unnecessarily large doses must always be considered, and it may be added that such a distinguished authority as Baginsky believes that 5,000 or 6,000 units are enough for an initial injection and that such a moderate dose need only occasionally be repeated.

And now as regards the *minimum therapeutic dose*. This may be taken as ranging from 1,000 to 2,000 antitoxic units. Unquestionably even such moderate doses, if given early in the illness, are of the greatest value. That was conclusively proved by the improvement in our results at a time when such doses were seldom exceeded. The smallest dose which I am in the habit of giving at the present time is 1,500 units, and this chiefly to cases which are more bacteriological than clinical diphtheria.

How far, in estimating the dose to be given, are we to be influenced by the *age* of the patient? So far as infants are concerned I seldom give more than 4,000 units at a single dose, and this should be an adequate amount when we consider the small size of the patient. But to children of over one year 6,000 units may be given without hesitation, always provided the circumstances of the case call for liberal dosage. Otherwise there is no advantage in graduating doses according to age. It is in children that the disease is most fatal, and, if anything, they require more antitoxin than adults for corresponding lesions. It is this fact that seems to contraindicate a method of dosage based on the *weight* of the patient. Otherwise on strictly scientific grounds it would appear the most reasonable system, for, as Park points out, it is obvious that the smaller the individual the greater, after a given dose, is the amount of antitoxin in each cubic centimetre of his blood.

The *day of illness* on which the patient comes under treatment should, I think, also be considered. For corresponding tonsillar lesions a dose of 1,000 units on the first day may do more than one of 4,000 on the fourth. As a rough rule I give a patient, seen on the second day of illness, who presents lesions on the tonsils only, 3,000 units, increasing the dose to

4,000 if he does not come under treatment until the third day. While such a method is, no doubt, illogical if we cannot expect to detach toxin already combined with the tissues, it none the less appears to work very well in practice. I doubt if we can expect much result from injections first undertaken on the sixth day and after, indeed we might almost consider the fifth day the turning-point (see Table E). But I agree with Rolleston that serum should always be given however late in the illness, and occasionally it appears to exercise a really beneficial action. In late cases, however, I give one dose, usually large, and seldom push the serum with repeated doses.

Of more importance still is the *situation and extent of the lesion*. If the false membrane involves the pillars of the fauces, the uvula, or the posterior pharyngeal wall, much more antitoxin will be required. About 1,000 units extra may be added for any of these situations. Thus a case in which the tonsils and uvula alone are patched, and which comes under observation on the third or fourth day, might receive about 6,000 units, and should the membrane be well forward on the palate 8,000 might be given with great advantage. Cases which, in addition to faucial lesions, present laryngeal symptoms should never receive less than 6,000 units, and if the nose is involved it is well to increase the dose up to the maximum. Large doses must also be given if the false membrane is situated on the conjunctiva or vulva. It is my usual custom to give purely laryngeal cases 6,000 units, whether there is much dyspnoea or not. All these suggestions must be taken as referring merely to the initial dose, although in many instances it will be found that no more serum will be required. As regards purely nasal diphtheria distinction must be made between those cases which have merely a dirty chronic discharge containing bacilli, and those which present actual membrane accompanied by well-marked faucial lesions and toxic symptoms. The first class hardly requires serum at all, the second must be treated with large amounts.

This reminds us that, in estimating the dosage, it is highly necessary to pay due attention to the effect which the toxæmia is having on the patient. Two persons, suffering from corresponding lesions, may show very different degrees of toxæmia. A patient who is pale, drowsy, and prostrated, who has large masses of glands round the neck, or who has much albuminuria, will require a much larger dose than one who presents none of these signs. All such bad symptoms must be carefully taken into account, and it is to these patients, and to those with persistent dyspnoea, that we expect to be obliged to administer the maximum dose and to repeat it at suitable intervals.

While, within limits, our object is to give one dose which will be sufficient

to effect the desired improvement, and while, if patients were only treated early enough, second doses would probably never become necessary, we frequently meet cases in which we cannot expect a single dose of 10,000 units to check the further production of toxin. How soon, then, is the *dose to be repeated*? This will vary with the circumstances of the individual case. If the patient is extremely ill, a second injection may be given in from six to eight hours. If the symptoms are less urgent the interval may be extended to twelve or even twenty-four hours. For ordinary cases, in which no special danger is apprehended, the twenty-four hour interval works very well. If, on examination of the patient on the day after treatment is commenced, there is no diminution in amount of membrane visible in the throat and the general symptoms have not improved, it is necessary to repeat the dose. Any extension of membrane in the face of treatment, a contingency extremely unlikely to occur unless the severity of the attack was underestimated when the first dose was prescribed, must be met with a large second dose, certainly with one larger than the first.

It is only right at this point to allude to another side of the question and to discuss the *theory of the single dose*. Park, whose admirable and helpful work on this subject commands the greatest respect, holds the view, based on both laboratory and statistical evidence, that 'amounts of antitoxin beyond 25,000 units in a child and 50,000 in an adult are absolutely unnecessary and useless; and that an initial dose of 10,000 in a child and 20,000 in an adult is probably sufficient for the whole course of the disease'. The object is to get antitoxin quickly into the blood to neutralize the toxin, and, especially when given subcutaneously, the active part of the serum passes into the blood slowly. The injection is being absorbed for days, and it takes 48 hours before a concentration of $3\frac{1}{2}$ units per c.c. of blood is attained. To give repeated doses is only to delay getting the required amount of antitoxin into the blood. One massive dose will attain the object desired much more quickly.

I fear that my own practice is open to criticism in this particular. No doubt large doses have not nowadays the disadvantages which they had before high potency serum was available. But to divide the 20,000 or 30,000 units, which one imagines a case will probably require, into two or three doses gives an opportunity for economy should the symptoms clear up rapidly and is not, I think, likely to prejudice the patient if the interval is a short one and the whole amount given is injected within from 24 to 48 hours. It is, moreover, more satisfactory to the medical attendant, and possibly to the patient's friends, to go on actively treating if improvement does not manifest itself, than to have to make an estimate of what is sufficient

and then sit down and wait for the single dose to act. I accept without hesitation the results of Park's interesting experiments, which show conclusively that an animal receiving 15,000 units in one injection exhibits after 18 hours more than thrice the amount of antitoxin in the blood than another which receives four doses of 5,000 each at intervals of eight hours. But it is difficult to follow new ideas, however well substantiated, after long clinical experience, reasonably satisfactory, of another method. The reader must be the judge and select his method for himself. If I were starting my diphtheria experience now I should probably follow Park, but I sympathize with McCollom's view that dosage must be decided by observation of results in actual cases; and those results after all, in spite of statistics, must be a matter of personal opinion. Of one point I am quite convinced, and it does not seem to me to altogether tally with Park's view of the delayed action of antitoxin. Serum appears to me often to give results at once. If not, how can we explain the fact that there is no extension of the local lesion after an adequate dose has been given? In twenty-three years I have never seen implication of the larynx supervene in a patient who had not that lesion on admission. Glands, moreover, are most appreciably reduced in some cases within 24 hours, and a profuse nasal discharge sometimes ceases, and is often ameliorated, in the same time, and that after subcutaneous injection only.

As to the *total amount of serum to be administered*, continued injections at short intervals are required until improvement has taken place. So long as there is membrane on the throat it is probably worth while to push the treatment, unless, of course, it is obviously and rapidly disintegrating. In severe naso-pharyngeal and laryngeal cases it may be necessary to give in all 40,000 units or even more. My own largest total dose has never exceeded 64,000 units, a comparatively low figure when compared with the enormous totals reported by McCollom and others. In not a few cases there is no visible improvement until the patient has received over 20,000 units, and there is no doubt that, when a diphtheritic broncho-pneumonia is supervening in a laryngeal case, much is to be gained by pushing the serum till the respirations and temperature fall. Except in this class of cases, a fall of temperature is not to be regarded as a sign to stop the treatment, unless, indeed, the patient is much improved in other respects. The worst instances of diphtheria often run their course with the temperature normal or subnormal (Fig. 48).

Importance of early treatment. In conclusion it may be said that the most important point to be observed is to give the serum at once. The necessity for early dosage cannot be over-estimated. It is fatal to wait for the result of

cultures, except perhaps in the case of the most trivial of throats. When once a case is suspected, an injection should be given. The diagnosis can be made afterwards. Even a small dose, for instance 1,500 units, may be of the utmost value in checking the spread of a membrane, and can do the patient no harm whatever. A few hours may make an enormous difference in the prognosis of any given case. A table (Table E) is appended, showing how the percentage mortality increases with the postponement of the first injection. The progressive rise in the mortality rate is shown with sufficient clearness, and the importance of administering the first dose of antitoxin not later than the third day is well emphasized. It should be explained that, in constructing this table, the history of the case as given by the parents was accepted. All the fatal cases attributed to the first day were laryngeal, and it is extremely probable that the illness was of much longer standing than was alleged. I have never seen a fatal result in a case which developed in hospital, and in which injection was practised on the first day of the disease.

TABLE E

TABLE SHOWING MORTALITY OF DIPHTHERIA ACCORDING TO THE DAY ON WHICH SERUM WAS FIRST INJECTED IN 8,591 CONSECUTIVE CASES

<i>Day of Illness.</i>	<i>Patients.</i>	<i>Deaths.</i>	<i>Percentage of Mortality.</i>
First . . .	329	5	1.52
Second . . .	2,269	77	3.39
Third . . .	2,407	165	6.85
Fourth . . .	1,612	176	10.91
Fifth . . .	911	136	14.92
Sixth . . .	416	54	12.98
Seventh . . .	320	53	16.56
Later . . .	327	50	15.29
Totals . . .	8,591	716	8.33

Some caution should be exercised in the administration of serum for the *treatment of relapses*. I was for long accustomed to withhold it altogether, except in virulent cases, on account of the exaggeration of the serum sickness which nearly always followed it, and usually appeared early. Now, the anaphylactic nature of these phenomena being recognized, all that is necessary is to desensitize the patient (see page 445), should it be deemed advisable to give an injection.

As regards the *mode of injection* the *subcutaneous* route originally universally employed is still probably that used by the vast majority of practitioners. The injection may be made in the flank or, as I was inclined to

prefer, into the loose tissue between the shoulder blades. The usual aseptic precautions should be taken and the puncture sealed with collodion and cotton-wool. For the last six years, however, I have ceased to give subcutaneous injections, and have adopted the *intramuscular* route for the great majority of our patients. This mode of injection, as recommended by Baginsky and others, has more than one advantage. The antitoxin is absorbed more rapidly, Park considers twice as rapidly, than when given subcutaneously. The injection is much less painful and can usually be given more quickly, and none of the difficulties or limitations of intravenous administration are encountered. It is true that, according to Park, there is not infrequent leakage from the muscle substance, but if that occurs the patient is as well off as if the injection had been subcutaneous. The muscle we prefer is the vastus externus, the needle being inserted on the outer aspect of the thigh.

TABLE F

SHOWING PERCENTAGE INCIDENCE OF PARALYSIS ACCORDING TO THE DAY OF FIRST INJECTION

Cardiac cases with no other form of paralysis are excluded.

<i>Day of Illness.</i>	<i>Patients.</i>	<i>Cases of Paralysis.</i>	<i>Percentage.</i>
First . . .	142	3	2.1
Second . . .	1,026	53	5.1
Third . . .	1,015	98	9.6
Fourth . . .	651	93	14.2
Fifth . . .	356	36	10.1
Sixth . . .	134	19	14.1
Seventh . . .	119	13	10.9
Later . . .	115	5	4.3
Totals . . .	3,558	320	8.9

This table shows how the paralysis rate increases in the first four days. The slight falling off afterwards is, no doubt, partly explained by the high mortality of the 5th, 6th, and 7th days, the patients not surviving long enough to develop paralysis.

The most effective mode, however, is undoubtedly that of *intravenous* injection. Dose for dose, when 2 units per c.c. of blood are obtained in six hours by the subcutaneous method, 20 units per c.c. are found present if the intravenous route has been used. Park, who gives these figures, also adds that whereas there is a slow increase of antitoxin with the first method there is a steady decrease with the second, though even after twenty-four hours there is a difference in favour of intravenous injection, 12 units per c.c. as against 6 after subcutaneous. This consideration, perhaps, may justify

my usual prescription in very severe cases of 10,000 units intravenously followed in 8 hours by 8,000 or 10,000 intramuscularly, a third dose being occasionally added. This would seem to secure a fairly high antitoxin content in the blood for some time. I limit intravenous therapy, however, to adults and older children whose veins allow the easy introduction of the needle. Small children with fat arms and collapsed veins require a dissection which in my opinion does them more harm than does the delay of absorption after intramuscular injection, as it can hardly be effected without either a struggle or an anæsthetic. In all cases in which intravenous injection is used the serum should be warmed to approximately blood heat.

While it is said that appreciable amounts of antitoxin can be absorbed from the rectum of a newly-born infant, and traces even from that of an adult, the administration of serum either by the rectum or the mouth need not seriously be considered as a therapeutic measure.

SERUM SICKNESS AND ANAPHYLAXIS. A certain percentage of our cases will present sequelæ which are apparently due to the injection of a foreign protein. They occur, indeed, after injections of normal horse serum and are in no way due to the antitoxic bodies contained in a therapeutic serum. They have been explained by Von Pirquet and Schick as an anaphylactic phenomenon and, although some of us might prefer to reserve the term anaphylaxis to those cases in which a previous dose of serum has been injected, no doubt the process is fundamentally the same. It may be assumed that antibodies to the foreign protein are produced, and that after an interval, which varies considerably but is often from 8 to 12 days, they have developed or accumulated sufficiently to interact with any of the horse serum which may remain in the body cells. The interaction produces an apotoxin which causes the symptoms of the serum disease. If, then, before

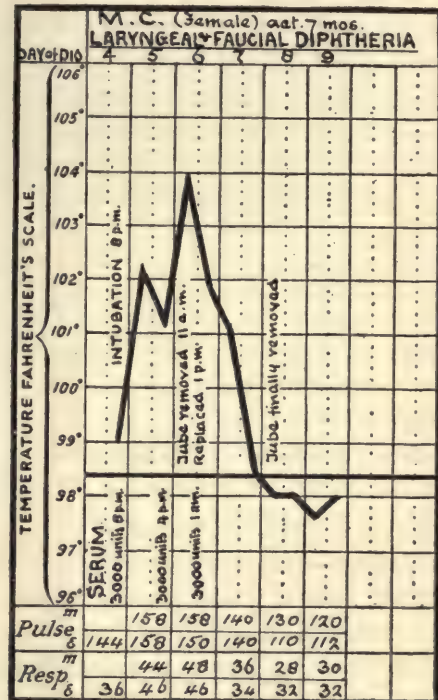


FIG. 49. A severe case of laryngeal diphtheria in an infant. Intubation. Note rise of temperature and respirations, suggesting a lung infection, and treatment by repeated moderate doses of serum. Recovery.

the requisite development of the antibodies the foreign protein in the horse serum has all been got rid of, no reaction occurs and no serum phenomena result. This explanation is in accordance with the clinical observation of Rolleston that serum reactions occur in direct ratio to the amount of serum given, the smaller doses being doubtless less liable to persist sufficiently long in the circulation. It appears to leave unexplained Rolleston's second observation, which accords with my own experience, that reactions occur in inverse ratio to the severity of the disease. We expect to meet with them chiefly in mild and moderate cases which have received very liberal dosage, though they may occur in any case. They have decreased very much in recent years, partly no doubt owing to better methods of preparation of serum, but also on account of the fact that high potency antitoxins can be given in sufficient doses in a much smaller bulk of serum.

The principal features of this **serum sickness** are firstly various forms of rashes, secondly pyrexia, and thirdly joint pains. These may occur separately or in combination. Of the less prominent manifestations may be mentioned slight œdema, affecting usually the loose tissues such as the eyelids or prepuce, but also occasionally seen in the hands and feet. A general puffiness of the face is not at all uncommon. Many writers lay great stress on adenitis as being a frequent symptom, the glands draining the site of injection being most distinctly affected. Occasionally the more usual manifestations are accompanied by some congestion, or even patching, of the fauces. This form of sore throat is most commonly observed in the more severe examples of the condition. Lastly, it is important to recognize that vomiting may accompany or precede these different serum phenomena. It is not, however, at all common.

The most obvious and important of the symptoms are undoubtedly the various forms of *rash*. While rashes of a mixed character are frequently observed, four main types are generally recognized.

1. *Urticarial rashes*. If we include in this group all cases which present a superficial resemblance to urticaria, these rashes are perhaps the most common of all. Large irregularly shaped scattered blotches appear on the skin, the neighbourhood of the site of injection being usually affected first. In many cases true urticarial wheals rise in the centre of the blotch, and, if so, there is intense itching and irritation. Sometimes, however, while the appearance and distribution of the rash resemble urticaria, no wheals appear. The rash is often very profuse and fresh plaques may continue to come out for two or three days. Occasionally, on the other hand, only two or three blotches are noticed, and may remain visible for less than



A SERUM RASH OF THE URTICARIAL TYPE.

twelve hours. The most common time for this form of rash to appear is from the eighth to the eleventh day after injection.

2. *Multiform erythema*. This type of rash is also extremely common. Often it is circinate in its arrangement, perhaps more frequently it assumes the character of large patches mixed with a scattered and somewhat morbilliform erythema. Different parts of the body may present quite different appearances at the same moment. The face is almost invariably blotched and often puffy. In colour the rash is usually a somewhat bluish pink.

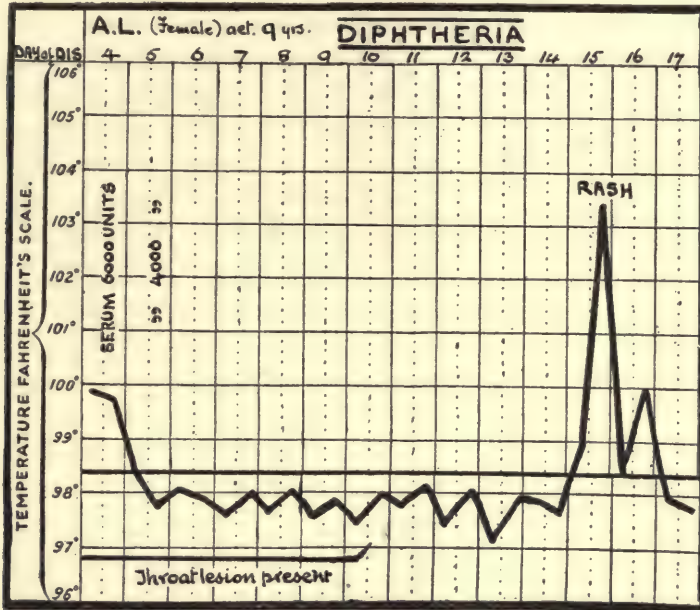


FIG. 50. A case showing an elevation of temperature in convalescence, which was due to the effects of serum, and was accompanied by an urticarial rash and joint pains.

It may change much in appearance from day to day, and sometimes lasts for over a week. Occasionally it becomes hæmorrhagic and the skin may be left deeply stained. This, however, is not at all usual. A mixed erythema often succeeds an urticarial eruption after two or three days' interval.

3. *Morbilliform rashes* are said to be common, but I have seen very few which resembled the rash of measles sufficiently closely to cause trouble in diagnosis. The relative frequency of the different types of rash probably depends to some extent on the particular serum used, which, no doubt, accounts for differences of opinion on this point. Sometimes the whole body, including the face, is covered with a uniform measly rash. As the conjunctivæ are liable to be congested in almost any variety of serum sickness,

and as puffiness of the eyelids is not at all uncommon, the resemblance to measles is, at times, sufficiently striking. But catarrh is conspicuous by its absence, and the buccal mucous membrane shows neither stomatitis nor Koplik's spots. There may, moreover, be a complete absence of fever. Even if it is present, the chart shows no prodromal rise of temperature. The rash, again, is not raised as much above the skin as is the case in measles, and, a point of much less diagnostic value, it often starts from the site of injection, and not on the face.¹

4. *Scarlatiniform Rashes.* It is, I think, beyond all question that serum rashes are not infrequently of a scarlatiniform type. Some writers would regard all such rashes as instances of true scarlatina, but, while the possibility of this infection must always be carefully considered, it is only occasionally the cause of the rash. The skin may present merely a uniform erythematous flush, which only superficially resembles the scarlet fever exanthem, or, on the other hand, there may be definite punctation, in which case the skin appearances are absolutely indistinguishable from those of scarlet fever. Rashes of this type usually occur early, that is to say the majority of them seem to appear from the second to the sixth day after injection. I have been accustomed to associate them with particular batches of antitoxin. Like the other varieties of serum rash, they may, or may not, be accompanied by pyrexia, and sometimes, though rarely, arthritis is present.

The *differential diagnosis* of these rashes from scarlatina is one of the greatest troubles of fever hospital life. It must always be recollected that scarlatina may at any time break out in a diphtheria ward. Even in private practice the appearance of such a rash, so soon after injection, often well within the limits of a scarlatinal incubation period calculated from just before the date of isolation, admits the possibility of the condition being in reality due to a coexisting infection. As regards diagnosis, those rashes which show no punctation should give but little trouble. In considering those which are definitely punctate, I am accustomed to lay most stress on the absence of constitutional symptoms. A rash, unassociated with the slightest suggestion of fever, or with such signs as headache, vomiting, or shivering, is probably due to serum, however closely it resembles the scarlatinal exanthem. On the other hand, rises of temperature, even so moderate as 99° F., increase the possibility of the case being one of mild scarlatina. Fever, indeed, though perfectly compatible with a mere serum manifestation, should always arouse suspicion. Even in cases with a marked febrile reaction, however, the presence of a single urticarial or erythematous blotch on the

¹ Davidson, who has endeavoured to demonstrate that these three varieties of rash differ in their incubation periods, and to some extent in their symptomatology, suggests that they may be due to the three proteins of horse-serum, englobulin, pseudoglobulin, and albumin.

face, or elsewhere, points clearly towards a diagnosis of serum sickness, as would also the appearance of definite joint pains on the first day of the eruption, a date which is distinctly early for scarlatinal arthritis. Well-marked fever, without such signs, would strongly predispose us to a diagnosis of scarlatina, and this view would be much strengthened if initial vomiting and sore throat have been noticed. Here again we are confronted with the difficulty that the throat is sometimes affected in serum sickness, and that vomiting, though rare, is occasionally met with. But the conjunction of symptoms so suspicious with a definite punctate rash, and more or less pyrexia, should justify a diagnosis of scarlatina. Two other points may be mentioned. The condition of the tongue and the manner of its peeling should be closely watched. When the changes characteristic of scarlatina follow in orderly succession, and ultimately a bright red 'strawberry' tongue is left, the mere fact that the patient has had no rise of temperature does not stop me regarding the case as one of scarlatina. In doubtful cases, when the tongue remains furred for an indefinite period, the presumption against scarlatina is reasonably strong. Desquamation, even in serum rashes, may resemble that of scarlatina, but it is much less definite and usually does not involve the palms and soles. The diazo reaction is, so far as my experience goes, invariably absent in serum rashes. If the urine, then, gives this test, the presumption is in favour of scarlatina, in which disease the reaction not infrequently occurs.

It is obvious, then, that the distinction of such a condition from scarlatina may be a matter of extreme difficulty, and I must confess that I have very little confidence in my own powers of diagnosis in these cases. The safest plan, indeed, is to promptly remove from a diphtheria ward all patients who develop scarlatiniform rashes. If no pyrexia and no constitutional symptoms are present, isolation in a side ward, with suitable precautions, such as the wearing of a special overall cloak by the nurses, is probably sufficient. If fever and other suspicious symptoms are present, removal to an isolation block is highly desirable. It is inadvisable to place patients in a ward in which they are exposed to the infection of scarlatina, unless the tongue is extremely characteristic and the desquamation typical. I have, on more than one occasion, seen persons who, to all appearance, were indistinguishable from cases of scarlatina, contract that infection shortly after their admission to a ward containing patients suffering from scarlatina.

The rashes due to serum may appear at almost any moment within four weeks from the day of injection, but the period between the seventh and eleventh days, inclusive, seems to be the most usual *time of occurrence*. I have seen blotchy rashes as early as twelve hours after injection, but it is seldom that a rash is seen before the third, or after the eighteenth day. Between

these limits, however, their occurrence is fairly common. In the series noted in the appended table, a large number of those occurring from the second to the fifth day were scarlatiniform, and it is just possible that a few cases of real scarlatina may have been included. It will be noted that joint pains, either with or without rash, are most frequently met with from the tenth to the twelfth days.

The same table gives some idea of the *percentage incidence* of serum phenomena. In this series about one-quarter of the patients suffered from antitoxin sequelæ. This percentage appears low in comparison with the figures reported by other observers. In a series of Brownlee's 47 per cent. of the patients injected developed serum sequelæ, and Rolleston reports that urticarial rashes occurred in as many as 66 per cent. of his cases. But in a second series of my own, consisting of 1,369 consecutive cases, only 238, or under 18 per cent., had rashes or joint pains, and it is probable that these differences may be accounted for by the peculiarities of the serums employed. The table and the above figures refer to cases before 1909. Of recent years the incidence has been much less and joint pains have been relatively less frequent. In 1916 and 1917, of 1,608 patients treated only 8.2 per cent. developed serum sickness.

TABLE G

TABLE SHOWING DATE OF APPEARANCE OF SERUM PHENOMENA

<i>Day from injection.</i>	<i>Rash only.</i>	<i>Rash and pains.</i>	<i>Joint pains only.</i>	<i>Day from injection.</i>	<i>Rash only.</i>	<i>Rash and pains.</i>	<i>Joint pains only.</i>
1	0	0	0	14	8	0	1
2	4	0	0	15	8	2	0
3	9	0	0	16	3	1	1
4	27	0	0	17	4	0	0
5	17	0	0	18	3	1	1
6	17	2	0	19	0	0	3
7	25	1	0	20	0	0	0
8	28	4	0	21	1	0	1
9	37	1	1	22	1	0	0
10	27	4	1	23	0	1	0
11	15	6	2	24	1	0	0
12	7	3	1	25	1	0	0
13	12	2	0	26	0	0	0

This table illustrates the occurrence of serum sequelæ in 1,142 consecutive cases of diphtheria. In all 292 patients, or 25.5 per cent. of the whole, developed rashes, joint pains, or both combined. These figures, however, refer to cases treated prior to 1909, our present percentage being 8.2 only.

The table shows that *joint pains* only occasionally accompany the rash. They are even less frequently seen alone. There is not usually much swelling in the joint, but considerable tenderness is often noticed, and there may be



A



B

SERUM RASHES.

A—A multiform erythema with some tendency to circinate arrangement.

B—Erythema best marked at site of injection. Some spotting on trunk and arm.

great pain on movement. It is probable that some of the instances of unexplained *pyrexia* which are noticed in the convalescence of diphtheria are due to the serum. Marked glandular enlargement in the neck is not, as a rule, seen except in severe cases of serum sickness. While severe sore throat is rare, occasionally the fauces may be sufficiently affected to give the impression of a relapse of diphtheria. Very rarely the inflammation is laryngeal, and may be sufficiently serious to require an intubation. It was at one time asserted that albuminuria was caused by serum injection. I find it difficult to believe that this is the case.

It has been suggested that the systematic administration of calcium chloride has a prophylactic effect on these serum sequelæ. So far as urticarial rashes are concerned, the drug may with advantage be tried either as a prophylactic or as a remedy. But, except for rashes in which so-called 'serous hæmorrhage' takes place, it is difficult to see that much benefit can be expected. As a rule our treatment must be local and palliative. Occasionally the joint pains are so severe, or the skin irritation so intense, that an opiate is advisable. It is true that opium may make a rash temporarily worse, but, if a good night's sleep is secured, that appears a matter of little moment.

In exceptional circumstances *abscesses* may occur at the site of injection. These must be regarded as being due to sepsis.

True Anaphylaxis. I prefer, perhaps illogically, to reserve this term for those cases in which a patient, as the result of a previous injection of horse serum, has been rendered hypersensitive before he comes under treatment. In such a case it may be assumed that either the antibodies already present in the blood combine at once with the injected serum and that the resulting poisonous substance causes immediate shock or a very rapid development of the more usual serum phenomena; or that, as might be expected if the interval has been somewhat longer, the antibodies, though not actually present at the moment of injection, are more quickly produced from cells which have been on a former occasion stimulated to their production, and are therefore, by early combination with the serum, capable of causing the supervention of serum sickness to be accelerated. Anaphylactic symptoms occurring within 24 hours are termed *immediate*, though it might be better to retain that title for cases of anaphylactic shock, while those which appear within seven days have been described by some writers as *accelerated*, a term which would appear more appropriate for the occurrence of serum sickness within two or three days of injection.

There are, perhaps, fifty or fewer examples in the literature of sudden death following serum injection, and the accident seems most usually to

have occurred in children suffering from status lymphaticus or persons who have been subject to asthma. In the less severe cases of shock, which terminate in recovery and which have been much more frequently observed, the patient is collapsed and suffers from distressing dyspnœa. The face becomes cyanosed and œdema appears rapidly. The pulse is soft, small, and rapid. Usually a rash, most frequently urticarial, sometimes scarlatiniform, develops within half an hour. It may, indeed, be observed much earlier. Rashes seen in these immediate, as also in the accelerated, reactions are usually very profuse and extremely irritating, and the discomfort of the patient may be extreme.

Of recent years the large number of soldiers who have been wounded and received anti-tetanic serum as a prophylactic has increased the proportion of persons in the country who have been sensitized to horse serum. The more extended use, moreover, of prophylactic injections of anti-diphtheritic serum has unquestionably made serious consideration of this problem a real necessity. It is most undesirable that serum treatment should be withheld, or unduly postponed, on account of risks which often seem to be exaggerated by nervous practitioners.

It is well, then, to remember that, whatever is the case with laboratory animals, dangerous anaphylactic symptoms are very rare in man. I must have administered second doses after the necessary interval in several hundred cases and in not one has there been signs of anaphylactic shock, although in very many of them no precautions were taken. Early reactions, such as rashes occurring within 24 hours, often accompanied by severe arthritis and much œdema and by pyrexia frequently well marked and prolonged, have certainly been noted in an undue proportion of these sensitized persons, but on the other hand many of them had no serum sickness whatever. It is curious that the only two cases of shock after injection which have occurred at the City Hospital were in young children who, it was ascertained, had had no previous injection. Both cases were alarming, but in both the danger was over within half an hour and both must be regarded as due to a natural hypersensitiveness to horse serum. In neither was there a history of asthma. The œdema, dyspnœa, and rash—the latter in one case was scarlatiniform—were well marked in both.

It does not appear to be determined with any certainty how long sensitiveness will last after the sensitizing dose, but in some cases it would appear it may continue for three years or longer. On the other hand, it should be assumed to be present ten days after the first injection. Kolmer advises as a test scarifying the arm, as in ordinary vaccination, and rubbing in a drop of the serum, when, if the individual is sensitive, a local reaction occurs

within fifteen minutes. It would in any case appear advisable to desensitize all persons who are known to have had injections of serum within three years, and in particular all asthmatics, especially those who suffer from the form of asthma which is excited by the smell of stables or horses.

It is customary to attempt *desensitization* by the injection of a minute quantity of serum, 0.5 c.c., subcutaneously, and then give the therapeutic dose 4 hours later. It is true that cases where this method appears to have failed have been reported. Besredka advises injecting fractional doses every 10 or 20 minutes, gradually increasing the dose until a therapeutic amount has been given, but the simpler method which I have habitually employed for the last six years appears to be sufficient. In all these cases intravenous injection should be avoided, and the first dose should be subcutaneous, or at most intramuscular. The very slow absorption from the rectum has caused some to prefer that route, but, while no doubt desensitization may be attained in that manner, the patient must suffer from the delay in efficient treatment. An injection of atropine sulphate, say $\frac{1}{150}$ of a grain, is said to prevent anaphylactic shock, and a general anæsthetic has the same advantage. The general introduction of some different animal's serum, say that of the ox, for use for prophylactic injections only has been suggested by many authorities, and such a scheme would, if systematically carried out, diminish enormously the number of sensitized persons. As to the *treatment* of anaphylactic shock itself, the prompt use of stimulants, hot bottles, and hot fomentations over the heart, coupled with the intravenous injection of such drugs as atropine or adrenalin, should do something to prevent a fatal termination.

In conclusion, whatever view we may take of the risks of anaphylaxis, they provide no excuse for withholding serum. They are, after all, very exceptional, whereas the dangers of diphtheria are actual and present. I agree with Place that from the standpoint of practical medicine the risks of reinjection are very slight. Comby apparently takes no precautions whatever, and remarks that 'anaphylaxis, a very fine scientific discovery, should never have emerged from the laboratory where it took birth'.

LOCAL APPLICATIONS TO THE THROAT. Since the use of serum has become general these have taken a very secondary place in the treatment of diphtheria. Nevertheless, when we consider the foul and septic conditions often met with in the throat, it is highly desirable that some antiseptic treatment should be applied. As suitable a preparation as any is Löffler's solution of toluol in absolute alcohol. The prescription in use at the Edinburgh City Hospital consists of 36 parts of toluol, 60 of absolute alcohol,

and 4 of tincture of the perchloride of iron. To 100 c.c. of this solution 10 grammes of menthol may be added.

A pledget of cotton-wool, impregnated with this solution, is pressed firmly upon the false membrane, care being taken to avoid swabbing the unaffected parts of the throat. The toluol must not be used too frequently, thrice daily being quite sufficient. In the days before antitoxin was first introduced I satisfied myself that it was by far the most efficient local antiseptic for the throat. To assist in keeping the fauces relatively clean, and to remove loose shreds of membrane, boroglyceride and glycerine in equal parts may be used on a swab, at intervals of about four hours. Those patients who are able to gargle may do so with listerine, a dessert-spoonful to the tumbler of hot water, or with chlorine water, which, if not so pleasant, is said to be extremely effective. Sprays of peroxide of hydrogen, or corrosive sublimate in a 1-4,000 solution, may also be freely used both for the throat and nose. If the fauces are much inflamed and swollen great relief is often obtained from the inhalation of steam, with or without tincture of benzoin or creasote. The mouth must be kept scrupulously clean, and it is well to remove all loosely attached fragments of membrane. Douching or syringing may often be of great advantage. In nasal cases, particularly, the douche is very useful, forcible syringing of the nose being, on the other hand, much to be deprecated. In patients who have shown any tendency to hæmorrhage the throat and nose may be sprayed with a solution of adrenalin chloride, but too much must not be expected from any method of treatment in this type of case. Should the glands be much enlarged, and form a collar round the throat, fomentations wrung out of weak carbolic lotion (1-60 to 1-80), may be frequently applied, or the neck may be merely wrapped up in cotton-wool.

GENERAL MANAGEMENT. It is of the utmost importance that, from the moment diphtheria is definitely diagnosed, the patient be rigidly kept in the **recumbent posture**. Sitting up should not be allowed on any pretext whatever, and even the slightest exertion, such as reaching to a bedside table, should be strictly forbidden. Only one pillow, and that a soft one, should be allowed, so that the head is kept scarcely raised. If signs of heart failure supervene, the pillow must be withdrawn, and, if necessary, the foot of the bed elevated. A second pillow is added in about a fortnight in the average case, although it is advisable to wait longer before making this concession to patients whose pulse is poor. If the attack is a very slight one, the patient may be gradually propped up in bed from the middle of the third week, and, if no harm results, allowed to get up for an hour or two early in the fourth. In really severe cases, however, it is safer to keep him

in bed for at least six weeks, the tendency for the later forms of paralysis to appear at about the sixth week making such a precaution advisable. By that time, provided the pulse is satisfactory and there is no sign of paralysis, most patients may rise with safety, and a week later, if they can walk without difficulty and two consecutive negative cultures have been obtained from the throat, they may be allowed to leave hospital. Adults should not resume work, or children return to school, for some weeks later, and a complete change of air is often of great advantage. It may be added that the various forms of paralysis not infrequently seem to follow an increased employment of the muscles affected. Too much reading, for instance, may be responsible for strabismus or ciliary paralysis, and it is wise to forbid books altogether for the first few weeks of the illness.

Considerable attention to the question of **diet** is also necessary. In a depressing disease like diphtheria it seems reasonable to allow a liberal dietary, but it must be remembered that the forcing of too much nourishment on the patient may readily induce vomiting, and in no disease is vomiting to be regarded as more dangerous, owing to the strain which it may put upon an already debilitated heart. So long as the pyrexia persists, which, as a rule, is only for a few days, a fluid diet is amply sufficient. Should the throat remain painful after the temperature has fallen, the patient should still be restricted to liquid food. Milk and beef-tea, occasionally supplemented by a beaten-up egg, are in most cases adequate nourishment. In severe cases the diet must be kept as simple as possible, and if there is any sign of gastric irritability it is well to peptonize the milk. The main principle of feeding should be 'little and often', and, during the acute stage, something should be given at least every four hours. In moderate cases, after the pyrexia has subsided, soft solids may be given, such as milk puddings, oat-flour porridge, lightly-boiled eggs, stewed fruit, and jellies. Strong soups may at this stage take the place of beef-tea. The presence of albuminuria need not be regarded as any contra-indication to an increase in diet. If the food given is well tolerated, a rapid increase may be allowed, white fish and other solids, such as bread and butter, being given first, and shortly thereafter a reasonable quantity of butcher's meat.

Throughout the course of the illness, all patients, and children in particular, must be carefully watched for any sign of *difficulty in deglutition*, a complication which may appear with comparative suddenness, and which has been occasionally responsible for death by choking. Young children should be fed by a nurse, as otherwise they are apt to attempt to take too much at once. Should paralysis of deglutition occur, nasal feeding must be at once resorted to, if possible, but in some patients the local anæsthesia

makes it difficult to be certain of the position of the tube and rectal feeding will be found safer.

I believe that most patients who suffer from a moderate, or severe, attack of diphtheria are the better for a small daily allowance of *alcohol*. The disease is so typically depressing in its nature, and the tendency for the heart to fail is so marked, that some form of stimulation is usually advisable, if not absolutely necessary. The doses given should be extremely small, unless there is any special weakness in the circulation. In what we may term 'bacteriological cases', those which do not present very characteristic clinical appearances, the use of alcohol is uncalled for. Whisky or brandy are probably the most useful stimulants, but occasionally champagne may be of real value. In convalescence, such beverages as stout, or a glass of sound Burgundy, given with the meals, are often very useful.

Some form of *tonic treatment* is generally employed. Strychnine is, I believe, the most satisfactory tonic, and may be given freely. Its systematic use, however, unfortunately cannot be trusted to prevent either heart failure or paralysis, although I am inclined to think it lessens the tendency to both these complications. It may be given in from 1 to 3-minim doses, every four hours, according to the age of the patient, a child of ten or twelve readily tolerating the larger amount. After being used for about a week, it should be withheld for two or three days, and then resumed if necessary. Sometimes, if given too long, the pulse becomes unsatisfactory, and is actually improved when the drug is stopped.

In convalescence an iron tonic may be prescribed with advantage. Such preparations as Fellowes's Syrup, Easton's Syrup, and Parrish's Chemical Food are all useful.

Treatment of heart failure. The tonic treatment just mentioned has for its main object the prevention of cardiac failure. Too frequently it is unsuccessful, but that such drugs as alcohol and strychnine have some effect in warding off this danger there is, I think, no doubt whatever. When the pulse becomes weak and irregular there is but little more that can be done. Such drugs as digitalis and strophanthus are, in my experience, absolutely useless. I cannot speak with the same feeling of certainty about adrenalin, which sometimes appears to do the patient much good. Rolleston considers that if given early in severe cases it lessens the probability of a fatal termination by cardiac failure and, if there is anything in the theory of adrenal insufficiency, its administration should theoretically be beneficial in the 'vascular' type. But to get its full value intravenous injections at very frequent intervals would be necessary, and the difficulties of such a form of treatment are obvious. I have used it, by intramuscular injection,

extensively and, while it may be admitted that many patients seem to do well with it, like other drugs it works no miracles. On the whole I prefer camphor in oil in intramuscular injections of from 1 to 3 grains every four hours, but it must be regretfully confessed that no treatment seems capable of either preventing or improving a case of cardiac failure.

When the latter has declared itself, that is to say, when such symptoms as syncope, vomiting, or præcordial pain have occurred, the chances are all against the patient's recovery. In sudden collapse hot applications over the heart and injections of camphor, strychnine, or ether may be employed. The injection of normal saline, either into the rectum or subcutaneously, is worth trying. The patient as a rule rallies from his first collapse, but seldom survives a second or third, should they occur. All forms of treatment are extremely disappointing. The vomiting is sometimes held in check, the pain relieved, and the acute restlessness much lessened, by the cautious hypodermic injection of morphia and atropine in small doses. Occasionally the rest, so secured, has seemed to me to determine a favourable issue. Owing to the cardiac sickness the feeding must be entirely rectal. Iced brandy, or champagne, however, are often tolerated by the stomach when everything else is promptly rejected. When once heart failure has declared itself the foot of the bed should be raised.

Treatment of paralysis. The remarkably transient nature of many forms of post-diphtheritic paresis makes it exceedingly difficult to estimate the value of any particular form of treatment. Complete rest is requisite, and strychnine should be pushed. The use of antitoxin is not to be recommended at this stage of the disease, first because its value for this purpose is extremely doubtful, secondly because of the risk of anaphylaxis and severe serum phenomena supervening. Should there be any difficulty in deglutition, due to constrictor paralysis, the nasal tube should be used for feeding the patient. Much distress is sometimes caused by the collection of fluids in the back of the mouth which the patient is unable to swallow. Raising the foot of the bed is a useful procedure in such cases, as it prevents the saliva collecting over the larynx. Sometimes marked temporary relief is given by sucking out the fluid through a rubber catheter attached to a syringe, or the throat can be frequently swabbed by the nurse. Paralysis of this sort is usually so short lived that every means of palliation is well worth trying to tide the patient over the dangerous period. I have never satisfied myself that electrical treatment is of benefit in diphtheritic paralysis.

As regards allowing paralytic patients out of bed, when a slight palatal or ciliary disability has existed for two or three weeks, and there is no sign

of the graver forms appearing, the patient may be allowed to rise, but no undue exertion is to be permitted.

Treatment of laryngeal diphtheria. Admirable as are the results of operative interference since the use of antitoxin became general, our chief object, in hospital at least, will be to avoid operation. There is no doubt that much can be done to alleviate dyspnœa, and as, when a suitable dose of serum has been given, improvement may be expected in from twenty-four to thirty-six hours, every possible means of palliation should be employed. The most satisfactory therapeutic measure is, unquestionably, the inhalation of steam. The carping critic may suggest that it can do little good to place any patient in an artificial fog, or to fill the lungs of a suffocating infant with water. But all clinical experience goes to prove that, in acute laryngeal inflammations, steam gives more relief than anything else. It certainly diminishes the tendency to spasm, which is so largely responsible for acute attacks of dyspnœa, it assists in the expulsion of loose membranes, and, as it is easy to see from the manner in which children arrange themselves in bed so as to get the full advantage of it, it is of the greatest comfort to the patient. It is, however, often a difficult matter to give steam satisfactorily from an ordinary croup kettle unless a tent is used, and there are objections to any method which impedes the free circulation of air round an infectious patient. Two or three croup kettles, working at once and without a tent, can be trusted to supply an adequate amount of steam. For institutions a more efficient plan is that in use at the Edinburgh City Hospital, where the steam is laid on from the boilers and supplied to the patient through pipes on swinging brackets at each side of the cot, at a pressure reduced to about $3\frac{1}{2}$ pounds.

In addition to steam treatment, hot fomentations, frequently applied round the throat, are often very effectual. While medicinal treatment cannot be depended upon, the old plan of giving ipecacuanha wine, even to the extent of causing a vomit, has its merits for sthenic cases seen on the first day of their illness. For patients seen later, 5-minim doses of the wine assist the expectoration of loose membrane. Belladonna, if pushed, is often of value in relaxing spasm, but it must be given very freely if it is to be of any use. Every care must be taken to support the heart by appropriate stimulation.

As regards the **indications for operative interference**, they differ according to the circumstances of the case. In *private practice*, when the medical man cannot always be within reach, it is obviously safer to operate early. Should dyspnœa be well marked, with definite recession of the soft parts of the chest, should the patient be restless, or should even one severe

paroxysm of croup have occurred, it is wisest to perform tracheotomy at once. We can never predict when a second severe spasm may supervene, and in such an event the patient might suffocate before the medical attendant could arrive. It seems to me that a practitioner confronted by such a case has three alternatives. The first is to send the child to hospital at once, the second is to live in the house and not leave the patient for a moment, and the third, which is sometimes the only one possible for him to adopt, is to perform tracheotomy on the spot.

In *hospital practice*, on the other hand, it is well to wait as long as possible before interfering, with a view of giving the serum a fair chance. There is often no need to operate till the patient enters the third stage of croup, when the face becomes pale, the respiration more shallow, the recession less, and the pulse weaker and more rapid. The condition of the pulse, indeed, is my chief guide in deciding whether to interfere or not. Another point of considerable importance is the length of time the patient has been ill. We can take liberties in the first three days of a case of diphtheria which it would be foolish to risk a day or two later, by which time it is probable that the toxins have affected the heart muscle, and the chances of death from shock upon the operating table have, in consequence, increased. To sum up, then, in hospital interfere late, in private practice interfere early. Operation always has its dangers, and I think that there is more real satisfaction to be gained from dispensing with it than from the most brilliant results of tracheotomy or intubation.

Choice of operation. As regards these two methods it is well to recognize that intubation has now taken its place as a real rival of the more serious operation in hospital practice. The prejudice against it seems still very marked in this country, but it is almost universally practised in America and France. In my own view it is a hospital operation, and is not so well suited as is tracheotomy for private practice, unless, indeed, it is performed very early, that is to say, in cases which do not urgently call for interference. Such patients might be left with more confidence by the medical man if an intubation tube has been inserted, and, in the event of it being expelled by coughing, the chances are that no great harm will follow before aid arrives, or before the serum has had time to act. But in more severe cases the risk of a coughed-up tube cannot be lightly disregarded, and, unless a doctor is always on the spot, tracheotomy is a much preferable operation.

There is a belief in some quarters that, even in hospital, very severe cases are best treated by tracheotomy. I cannot, personally, recognize any distinction in the indications for the rival methods. In hospital it

should be only very severe cases which are interfered with at all, and I have never felt myself competent to predict that any given case will not be relieved by the intubation, which, as a routine, I practise first, and will obtain relief from the subsequent tracheotomy. In my experience, the number of cases unrelieved by intubation which recover after a subsequent tracheotomy is extremely small, even should the cutting operation be performed within half an hour of the intubation, and thus possess practically all the advantages of primary interference.

Intubation of the larynx. Although it is sixty years since Bouchut first appreciated the possibility of relieving dyspnoea by the introduction of a tube into the larynx, the operation of intubation, as we know it to-day, was not introduced till the year 1885, when O'Dwyer first introduced suitable instruments. These have been widely imitated, and to some extent modified to suit the tastes of different operators, but the only serious rival of the improved O'Dwyer tube is the short tube, suggested by Bayeux, and made by Collin of Paris. The tubes, originally made of metal, can now be obtained in vulcanite, and it is with this modification of O'Dwyer's pattern that I have obtained the most satisfactory results.

The instruments can be obtained complete in a box, and those made by Ermold of New York can be recommended, as being strictly of a pattern approved by O'Dwyer. The box contains seven vulcanite tubes graduated to suit the larynx at different ages, an introducer, an extractor, and a gag. Each tube is provided with a jointed obturator, the handle of which passes into the arm of the introducer and can be fixed there by a screw. The arm itself is a metal cylinder terminating in a spring and two projections, and can be moved forward by the pressure of the thumb, the projections pressing on the head of the tube, which is fixed by the obturator at right angles to the introducing instrument. The tube itself, when in position, is supported by its head on the aryteno-epiglottic folds and reaches within an inch of the bifurcation of the trachea. Below the head is a constriction, so that no undue pressure is put on the glottis or on the cricoid cartilage, and it is retained in place by a lateral swell which renders it more difficult to expel by coughing. The end of the tube is rounded off so that ulceration caused by pressure in the act of swallowing is avoided.

Intubation should not be performed unless the instruments for tracheotomy are at hand. Occasionally, though extremely rarely, membrane may be rolled up in front of the entering tube, completely plugging the trachea. The patient should be pinned firmly in a blanket and placed in the recumbent position. There is no justification for adopting the sitting position in a disease like diphtheria. The gag is then inserted on the left

side of the mouth, and the operator, standing on the right of the cot and well above the patient, introduces the left forefinger into the mouth and finds the opening of the glottis. To do this the epiglottis may have to be hooked up. The top of the finger should rest on the arytenoid cartilages. These, however, cannot always readily be recognized, and the best rule is to find the opening of the larynx and slide the finger back to its posterior margin. The tube is then passed along the side of the forefinger till it reaches the tip, when its point may be slid beneath it and thus rests directly over the glottis. Taking the utmost care to keep the instrument in the middle line, the operator then proceeds to raise the handle of the introducer, tilting the tip of the tube into the opening of the glottis. Half the secret of intubation is to remember to raise the handle sufficiently, as the impression given in performing the operation is that the opening of the glottis looks almost directly backwards. Then, allowing the tube largely by the weight of the instrument to fall into the larynx, and taking care to exercise no undue force, the operator sets it free of the obturator by pressing forward the cylindrical arm, and follows the head of the tube with his forefinger, pushing it firmly home, when it is at once partially covered by folds of mucous membrane. Occasionally a spasm of the glottis resists the entrance of the tube, in which case, always provided the middle line is carefully maintained, a little gentle pressure may be exercised.

A string must always be looped through the hole in the collar of the tube, so that, if it falls into the oesophagus, it can be withdrawn. This can be removed by pulling on one end of the loop, though I prefer, personally, to leave it in position attached by a strip of plaster to the cheek. If this is done, it is well to use a string which cannot easily be bitten through, and banjo string (No. 6) will be found excellent for the purpose. It should not, however, be looped through the hole, but attached as a single string with a knot¹ on the end, which prevents it slipping through. It should be drawn taut, as otherwise a child, twisting his tongue round it, can extubate himself. The advantage of leaving the string in position is that a nurse can pull out the tube at once, should it become plugged, or should loose membrane, collecting below it, impede the breathing. Again, extubation, with the instrument provided, is much more difficult than intubation. The short French tubes can be 'enucleated', or pressed out, which is easy in the sitting position though more difficult if the patient is kept recumbent. The method consists in pressing firmly on the trachea, just below the larynx, with the thumb, while the other hand placed firmly

¹ The wire composing the outer cover of the string should be unwound for a short distance and the knot tied only with the silk thread which constitutes the core.

below the occiput simultaneously flexes the patient's head on his chest. This squeezes the tube out of position, and the patient is instructed to spit it out. The string is on the whole a handier method, and is, if fixed carefully, no trouble to the patient. On the other hand, it necessitates the arms being controlled in cardboard splints, as otherwise the patient would pull the tube out.

The length of time during which the tube should be worn is a matter of some interest. Some remove it for the first time in twenty-four hours, others leave it in position for as long as six days. The shorter period would be, doubtless, quite suitable for cases in which the intubation is a precautionary rather than a therapeutic measure. For patients whose dyspnœa has been severe before interference it would not be long enough, and the tube would probably have to be replaced, the patient being put to the distress of a second intubation which might well have been avoided. The psychological moment for removing the tube is from two and a half to three days from its insertion, and, always provided the temperature and respirations are normal, there is then a fair chance that the patient will escape further manipulation. If, however, there is still pyrexia and the breathing is rapid the tube will often have to be replaced, sometimes in a few minutes, sometimes after a couple of hours. It is rare for a patient who has breathed satisfactorily for as long as four hours to require a second intubation. Should, however, the tube be reinserted, an attempt should be made to remove it every second day. The greatest number of reintubations which I have performed in any successful case is fourteen, and the patient in question, after wearing a tube for four weeks, recovered satisfactorily, with no sign of ulceration of the larynx.¹ There is little advantage to be gained from a secondary tracheotomy undertaken to dispense with an intubation tube. It is better to persist with the latter, especially as light vulcanite tubes can be worn without damage for long periods. The cause of a retained tube may be either adductor spasm, due to atrophy of the abductor muscles, or subglottic hypertrophic laryngitis. Rogers has had great success in the treatment of these cases with special tubes made for the purpose, and fixed with clamps or a screw plug inserted through a tracheal opening. With such an arrangement the tube cannot be coughed out, and the patient can visit the medical attendant at suitable intervals. Cases of patients who wore such a tube for over two years without being able to dispense

¹ But a child still in hospital, first intubated two years ago and subjected to over eighty reintubations, has now entirely dispensed with her tube for fourteen weeks with no sign of dyspnœa. Some degree of stenosis persists, but she appears likely to make a complete recovery.

with it, and who finally made a complete recovery, have been reported. At the time the first edition of this book was published I had had practically no experience of permanent difficulty, but in a consecutive series of 268 cases five examples of laryngeal stenosis have since occurred, a proportion of 1·8 per cent. It is interesting to note that two of these cases were intubated for causes other than diphtheria. The cause of the obstruction was subglottic fibrous stenosis apparently due to ulceration from pressure of the tube, and although in one instance the tube had been worn for 9 weeks, in two of the others tracheotomy had been performed after 6 and 9 days respectively. Damage resulting in stenosis may, then, occur comparatively early. On the other hand, stenosis may not become apparent for some weeks after extubation. Two of the five patients above mentioned showed no respiratory difficulty at the date of their discharge from hospital. It is possible, then, that statistics giving the percentage of stenosis following intubation, which in a series collected from the literature by Logan Turner varied from 0·3 to 6 per cent., may not always include all the cases which suffer. In this country intubation is so little practised that we have few opportunities of studying the management of these cases of stenosis, and the fact that few laryngologists are accustomed to deal with them is perhaps an argument in favour of selecting tracheotomy as an operation, though it must be remembered that 'retained tubes' are met with also after that operation.

The use of steam in moderation is an advantage during the first few days in which the tube is worn, and while there is still a chance of it becoming clogged with tough mucus. Nasal feeding should be always employed, although some patients swallow soft solids extremely well, and Place considers that swallowing in the sitting position is quite satisfactory. I noticed, however, an immediate improvement in my results when the nasal tube was used exclusively. The only exception to this rule is that a little dilute whisky and water may be given by the mouth as, by exciting some coughing, it assists in keeping the tube clear. When the time has come to remove a tube it is advisable to make the attempt in the morning, as the breathing is always liable to be more difficult at night. The administration of belladonna in full doses during the previous twenty-four hours helps to lessen the natural tendency to spasm, and this may be combined with five drops of laudanum an hour before extubation. There is always a better chance of removing the tube for good and all if the patient is sleepy and free from nervous excitement. The older the child the more likely is nervousness to manifest itself. In cases of retained tube—'tubards' as they are called in France—it is often of advantage to have the patient as much as possible in the open air, to improve the general condition and soothe the nervous system.

A secondary tracheotomy will be necessary if the relief given by intubation is inadequate. In my experience it has usually been performed within twelve hours of the first intubation. The results cannot be expected to be as good as those of primary tracheotomy, for it is obvious that the obstruction is usually beyond reach. Less than half of such cases recover.

As regards intubation itself, for about 10 years the death-rate at the City Hospital was about 28 per cent. Since 1912, however, my results have not been so good, the type of diphtheria in the city being much more severe. At present the mortality is over 40 per cent., and to judge from the returns of some of the great American hospitals such a figure is, after all, not very unusual. It does not, however, compare very favourably with the tracheotomy results of some hospitals in this country, and I am at present considering whether in diphtheria of the severe type the latter operation may not give us more success.

Comparison between intubation and tracheotomy as an operation in hospital. We have seen that intubation hardly lends itself to private practice on account of the difficulty in replacing a coughed-up tube. In hospital, however, it has great advantages. It permits the patient to breathe *per vias naturales*, and there is therefore less chance of pulmonary sequelæ. A cutting operation is avoided, and there is no difficulty in obtaining the consent of the parents. No scar is left as a result. No preparation is required, and the patient is, as a rule, relieved in a few seconds. Tracheotomy, on the other hand, theoretically should give better rest to the affected parts, and should the tube become dislodged it can be replaced by a nurse. Membranes, moreover, can often be extracted through the wound both at the time of operation and after. Statistics are of little use in estimating the value of the rival methods. The results obtained must largely depend upon the condition of the patient at the moment of interference, and there is a tendency in some quarters to operate upon patients who would probably recover if left alone. On no other grounds can we explain such mortality rates as 5 per cent. for cases of intubation. There is a great difference of opinion whether membranes are expelled more easily by one tube or the other. The tracheotomy canula should, theoretically, allow larger pieces to be expelled. The intubation tube, on the other hand, certainly allows more vigorous and natural coughing. The danger of plugging of the tube under these circumstances has, I think, been exaggerated. At the worst, a tube which becomes plugged in this manner is usually expelled, and in any case, if the string is left attached, can be pulled out by the nurse. The danger of rolling up membrane in front of a tube in the act of intubating, and so plugging the trachea, is a more real one. It is an accident which has happened on several occasions in my experience, always, fortunately,

without fatal results. The great disadvantage of intubation is the amount of trouble it often gives to the medical attendant, who is practically tied to hospital, unless some other expert is available. In conclusion it may be said that, if the opportunities of becoming expert at intubation are few, the practitioner will be wise to prefer tracheotomy. The latter operation gives better results in the hands of the novice.

Tracheotomy. If it is decided to perform tracheotomy, it is well, unless the patient is obviously at the last gasp, to spend a few minutes in preparing the skin of the neck and chest for operation. Chloroform should, as a rule, be given. It is well tolerated if the patient has not been ill for more than three or four days. The risk of death on the table becomes greater with each succeeding day of the illness. For a patient who seems moribund an anæsthetic is unnecessary, and when there is a history of five or six days' illness, and the patient is very pale, eucaïne may be used locally for the skin incision. If a general anæsthetic is not employed, the child should be immobilized by a blanket wound round the limbs and trunk up to the level of the nipple. A rolled sheet, or a sandbag of a suitable size, about six inches in diameter, should be placed beneath the shoulders. The head must be held firmly by an assistant, who is instructed to keep the chin steadily in the middle line. A special tracheotomy rest, with side-clamps to hold the head in position, can be obtained for this purpose. The operator, standing on the right of the patient, then satisfies himself as to the position of the cricoid cartilage, and having discovered this anatomical point is careful not to lose it. Steadying the larynx between the thumb and middle finger of the left hand, with the forefinger resting on the lower margin of the cricoid, he then makes a skin incision downwards from the tip of the finger, taking the greatest care to keep the middle line. The length of the incision is a question on which there is some difference of opinion. About an inch and a half should be sufficient ; otherwise stitches will be required, and, if they give way, the tube has not the same support when it is finally in position. On the other hand, some prefer a very free incision, which has its advantages if an elaborate dissection is performed. Once the skin is divided, however, many recommend a bold plunge into the trachea, which, indeed, is the best method if the patient is literally *in extremis*. Before, however, this is attempted the left forefinger is inserted into the wound, and the lower edge of the cricoid again localized. All the time the thumb and middle finger are steadying the larynx. Half the secret of success is not to let go the original hold of the left hand. With the tip of the forefinger in the wound and on the cricoid, a tenotomy knife can be plunged into the trachea, care being taken to keep the handle perpendicular, and to avoid the tendency to tail away the incision obliquely towards

the operator. If the plunge method is not fancied, a dissection down to the trachea must be undertaken, and it is well not to attempt to control the hæmorrhage which may occur. It is chiefly venous, and stops as soon as the tube is in position. Moreover, if the middle line is scrupulously kept, it is usually trivial. To attempt to put on artery forceps pulls the parts out of position and increases the difficulty of the dissection. When the trachea is exposed, it is necessary to see that its covering aponeurosis is thoroughly divided. Otherwise, button-holes in this membrane may lead to false passages when the introduction of the tube is attempted. The trachea is opened by an incision from the point of the index-finger through the first two or three tracheal rings. A common fault is to make this incision too small at the first attempt, the noise made by the air hissing through the opening suggesting that the orifice is larger than it in reality is. The trachea once incised, the wound must be held open by trachea dilators, or in an emergency by the handle of the knife held crossways. No attempt should be made to insert the tube till the breathing is comparatively easy. If there is much hæmorrhage, the foot of the operation table should be raised to prevent the blood trickling down the trachea. Occasionally membrane is expelled through the wound. Often, on the other hand, none is to be seen. Should any be visible and appear to be loose, an attempt to remove it with laryngeal forceps should be made. When the patient breathes easily the tube may be inserted, and should be held with its orifice pointing directly into the wound, and its body at right angles to the axis of the trachea. The lower end once in the opening, the tube is easily manœuvred into position, and tied by tapes passed through the openings in the shield and round the neck. A light gauze dressing, covered with gutta-percha tissue, is arranged round the shield. As regards the choice of a tube, Parker's pattern appears to be most in favour. As to size, it should be large enough to fit the interior of the trachea somewhat closely. A tube too small for the patient is seldom comfortable.

A steam tent is not desirable in the after-treatment of a case, but the air may, with advantage, be kept warm and moist by a croup kettle near the bed. The inner tube must be removed and cleaned occasionally, but, as long as the patient is breathing well, it is unnecessary to disturb him often. The wound may be dressed, and the gauze changed, twice in the twenty-four hours. The feeding should be carried out entirely by the nasal tube. If the expectoration becomes tough and sticky, the outlook is usually a bad one. Some good may sometimes result from spraying the trachea with a weak solution of bicarbonate of soda. Many patients, however, die with their small bronchial tubes literally plugged with tenacious mucus. A fall of temperature to normal and infrequent respirations are to be

regarded as good signs. They at least indicate that the most dreaded sequel of tracheotomy, broncho-pneumonia, has not occurred. An attempt should be made, if the circumstances seem favourable, to take out the tube in three days from the operation. The inner tube should be first removed, and the orifice of the outer tube plugged. If the patient breathes well, the latter may be also withdrawn for a few hours, a few folds of damp gauze being placed over the wound. Often, however, the tube may remain in for a week before the patient can dispense with it, and less frequently it may be months before the child can breathe without it. In cases of retained tube intubation may be tried and not infrequently proves successful. Or if nervousness is the cause of the unsatisfactory breathing when the tube is removed, a dummy tube, as recommended by Goodall, may be placed in the wound, but not in the tracheal orifice. Granulations below the wound are sometimes a cause of trouble. I have seen little advantage result from scraping them away, or from the use of caustics. Knyvett Gordon uses a large-sized tube for this complication, under the pressure of which the granulations may disappear. Should similar obstruction exist above the wound, intubation is the most satisfactory remedy.

It must never be forgotten that a child who has successfully recovered from either tracheotomy or intubation is not, strictly speaking, convalescent. It has still to face all the dangers inseparable from an ordinary attack of diphtheria.

PROPHYLAXIS. The most important point is the *isolation* of the patient and the careful disinfection of everything used by him. Spoons, crockery, and the like must be set apart for special use, and frequently boiled. The isolation should be maintained until at least two consecutive negative cultures have been obtained from the throat. A long time is often required before this is attained, although in probably more than half the cases the cultures will be found negative within a week of the disappearance of the membrane. Only a comparatively small minority usually harbour the bacillus after the fifth week is over, and the number of convalescent carriers detected after the ninth week is very small. It is large enough, however, to make the management and treatment of **carriers** a most important question. How are we to free the patient from bacilli or how long is he to be kept in hospital? As to the first of these questions it must be admitted that treatment generally appears inefficacious. The carrier is usually a child with large and ragged tonsils, and the bacilli probably lie in the crypts and are not easily reached by whatever antiseptic is employed. I have used many forms of gargle, but cannot feel that any one is more effective than the rest, a conclusion reached by Meikle, who made a special study of the question in a long series of cases at the City Hospital. The use of living cultures of

staphylococcus aureus as a spray has been recommended by some observers, and Rolleston has spoken of it with approval. We used it in about a dozen obstinate cases just before the war, but the results did not, at that time, appear to justify the continuance of a method which requires careful supervision and occasionally will cause pronounced inflammation of the throat. The number of cases so treated and reported in the literature is small, and in many instances the patients treated had not harboured bacilli long enough to merit the name of 'persistent carriers'. In some cases, however, both of my own and of others, improvement was striking, and I hope to test this method again. The lactic acid bacillus has been used in the same way, but the results are even less convincing. Of other forms of treatment of which I have no experience a 5 or 10 per cent. solution of nitrate of silver has been employed, surely a somewhat severe procedure, and competent observers speak well of kaolin, powdered and dried in an incubator and dusted freely over the tonsils, the theory being that it draws as it were the bacilli out of the crypts by purely mechanical action. Lastly, tonsillectomy has been advised, and is sometimes, though by no means always, effective in obstinate cases.¹ It is a wise precaution to immunize the patient first, or at least to test his immunity by the Schick reaction.

We have recently employed the steam spray with sulphate of zinc solution in all our troublesome cases, but so far there is no evidence that the period of hospital detention has been shortened.

The ultimate disposal of a persistent convalescent or healthy carrier is a problem of the greatest difficulty. My own practice is detention for at least 12 weeks in hospital, after which time the virulence of the bacilli is tested on small animals. Should they prove avirulent I allow the patient to go, advising the frequent use of antiseptic gargles. It is interesting that we have never had a return case traced to such a patient. Arkwright and Ledingham add the further advice that even avirulent carriers should be excluded from school and be forbidden to have the care of children. If, on the other hand, the bacilli prove virulent, hospital detention should be maintained for some months longer if necessary, and the question of tonsillectomy should be considered. I do not, however, recollect having to keep a patient for more than four or five months.

The isolation of the patient having been effected, cultures should be taken from the throats of all contacts, and proved carriers isolated. I cannot, however, say that this procedure, which has been practised for the last 10 years in Edinburgh, appears to have much effect on the incidence of

¹ Treatment with vaccines of the diphtheria bacillus has not been encouraging. Hewlett, however, speaks hopefully of the use of injections of diphtheria endotoxin, and I am arranging to make a trial of this method.

diphtheria, which has certainly not become less prevalent. The detected carriers may, of course, be either the cause or the result of the patient's infection; most frequently perhaps the latter has contracted his infection from one of them, as there is, no doubt, a very large number of persons who, immune themselves, harbour and distribute the diphtheria bacillus. We find in different years that a proportion varying from 10 to 15 per cent. of our scarlet fever patients are carriers of the diphtheria bacillus on admission to hospital.

The carriers being dealt with, disinfection carried out, and the milk supply investigated, it only remains to decide what to do with the contacts, whether they be carriers or not. The debated point is, should immunization be practised or not?

Immunization. There are two methods of immunization possible in the prophylaxis of diphtheria, the injection of antitoxic serum or inoculation with toxin-antitoxin mixture. The first of these confers merely a passive immunity of short duration, whereas the latter will give an active immunity which is likely to last for some years. But, as time is required to secure results by the second of these methods, it is not suitable for dealing with actual contacts, and for the purpose at present under discussion we must employ *prophylactic injections of serum*.

The argument used against this system of protection is that it causes the sensitization to horse serum of a large number of persons who at some later date may, if serum is given them for any purpose, develop acute anaphylactic symptoms. But we have seen that fatal anaphylactic shock is a very rare phenomenon and that the other manifestations are more distressing than dangerous, and I have no hesitation in recommending prophylactic injections, especially for small children and other close contacts, whether they are carriers or not. If, indeed, a severe type of diphtheria appears in a house or school I think it a dangerous waste of time to wait for cultures, although I freely admit that a secondary case, should it occur, is not likely to run much risk if detected and treated on the first day of illness. In our own wards, where the children are under an observation more constant than can be managed in a private house, I only give protective injections if more than two cases appear in quick succession in one ward, though I always inject detected carriers.

The protection conferred by antitoxic serum lasts in my experience for three weeks, and becomes efficient after about 24 hours. A few patients therefore will develop symptoms of diphtheria within a day of the injection. I have had experience of a large number, certainly over two thousand, of these injections, and only four patients showed signs of the disease shortly after inoculation, one within 12 and three others within 18 hours. Four

other patients contracted diphtheria, two on the 22nd day, one on the 25th, and one after 5 weeks. The dose given in every case was 500 units only, which is smaller than that usually employed in many American hospitals, in which prophylactic injection is practised as a routine on the admission of every patient. This small dose has proved in my experience effective, and serum sequelæ have been almost unknown, even a slight rash being regarded as a genuine curiosity.

In hospitals in which prophylactic injection is employed as a routine for all children admitted, the preliminary application of the Schick test, as described below, would be an advantage and would prevent many unnecessary injections. But the delay entailed is too great for such a method to be applied in the case of contacts with actual diphtheria patients.

An active immunity of considerable, perhaps permanent, duration can be obtained by the use of *toxin-antitoxin mixtures*. Such preparations can now be procured from the large drug firms. That such mixtures would produce immunity in animals has been known for a long time. In 1912 Von Behring applied the method to produce immunity in the human subject, and since then much work has been done, especially by Park and Zingher in New York, which has all been in favour of attempting to diminish the prevalence of diphtheria by systematic immunization by this means. The theory is that the mixture is not very stable and that, when injected, sufficient toxin becomes dissociated to stimulate the production of antitoxin. An L. + dose of toxin is that amount which, when mixed with one unit of antitoxin, will kill a 250 gramme guinea pig at the end of four days. The mixtures used vary from 50 per cent. to 90 per cent. of the L. + dose to each unit of antitoxin. Zingher recommends 85 per cent. to each unit, and states that a strong toxin should be used so that 1 c.c., the usual dose, should contain at least two and one-half almost neutralized doses of toxin. For infants 0.5 c.c. is given as a dose. Three injections are usually advised, and are given subcutaneously at intervals of 7 days. Local reactions of varying degrees of redness, induration, pain, and tenderness are observed, but are said to be very slight in young children. Some adults, especially those who show pseudo-reactions with the Schick test, may suffer from local and constitutional symptoms for about two days, and in Zingher's opinion this is to be attributed to susceptibility to the protein contained in the mixture.

The New York Board of Health is so convinced of the protection afforded by this method of immunization that it has made arrangements to supply the necessary injections free within its area, and it encourages the inoculation of all children, especially of those in homes, day nurseries, and milk centres. Children of from 1 to 5 years, who are the most susceptible, should especially

be dealt with, as should adults whose duties bring them into contact with diphtheria. Zingher considers that all infants of under 18 months should be immunized with three doses, irrespective of whether they give a positive Schick test or not. Older children and adults should first be subjected to the test and inoculation need not be resorted to should it prove negative.

The careful work of Zingher goes far to demonstrate that children show considerable immunity in the first six months of life and then remain very susceptible for some years, slowly developing immunity as age advances. There is much to be said, then, for tiding them over the susceptible age, even if the protection conferred by the mixtures is not permanent. Zingher suggests that not only is an active immunity such as follows other forms of vaccination produced, but that there is also an earlier development of a natural immunity that would otherwise have manifested itself more gradually. The presence of this latter factor would justify the hope that the immunity is likely to be more or less permanent, and that therefore there is some prospect of controlling diphtheria. I have had as yet no experience of the method, but propose to immunize the hospital nurses.

The Schick Test of Immunity. This reaction depends on the local irritant action of diphtheria toxin if it is injected intradermally in a susceptible person. Many people are protected by the presence of natural antitoxin, which has been demonstrated in measurable quantities in the blood of such immune individuals, and, when immunity exists, no reaction follows injection. The test may be used, then, to determine the susceptibility or immunity of a child or adult, a negative reaction indicating that a person is adequately protected against diphtheria and does not require prophylactic immunization. Again, when such immunization has been practised, the reaction affords a handy means of estimating its success and its duration. The test may also be used in diagnosis, notably to settle the vexed point whether a patient, presenting a nasal discharge containing bacilli, is in reality suffering from diphtheria or is merely a carrier. In the latter case the reaction would be negative. A positive reaction, on the other hand, leaves the question an open one.

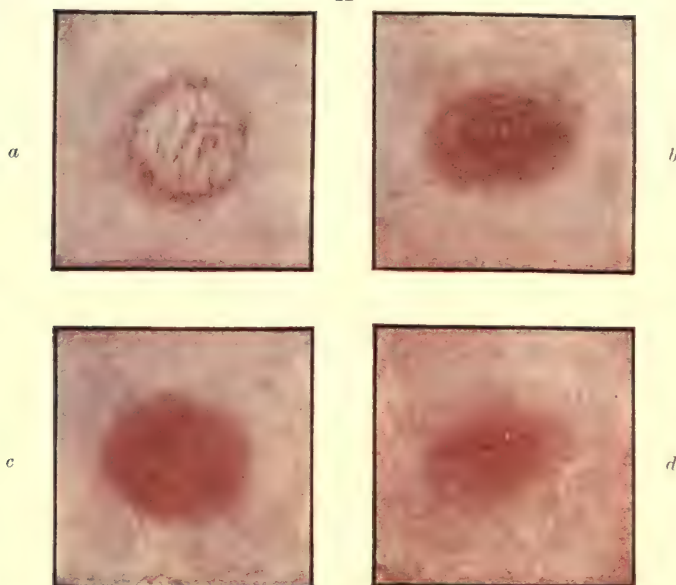
The injection should be made *into* the skin of the flexor surface of the forearm. A syringe of the type of the 1 c.c. record tuberculin syringe, provided with a fine needle with a sharp but short point, is convenient for the purpose. The dose of toxin injected is $\frac{1}{50}$ MLD. for the guinea pig in 0.2 c.c. of normal saline. An outfit can be obtained from at least one of the large drug firms. Zingher recommends for hospital purposes a supply of toxin which can be diluted for use as required. In making the injection care must be taken to give the dose into and not under the skin, and the proof of a successful

inoculation is the formation of a raised white wheal at the site of injection. If the *reaction* is positive a circumscribed area of redness and slight infiltration, measuring from 1.0 to 2.5 cm. in diameter, will appear in from 24 to 48 hours. The redness may persist for about a week and on fading leaves a brownish pigmentation and superficial scaling.

The true reaction must be distinguished from the *pseudo-reaction*, which may occur at all ages but is seen very much more frequently in adults. This would appear to depend on sensitiveness to the protein contained in the toxin, and will occur quite as readily if the toxin is inactivated by being heated at 75° C. for five minutes. Zingher advises that an injection of toxin treated in this manner should be made in the other arm at the time the test is applied and that the reaction should be thus controlled. A pseudo-reaction is usually less well defined at the margin, tending to develop a secondary areola around it. It is more infiltrated, and appears appreciably earlier than the true reaction, being often at its best after twenty-four hours. It, moreover, shows much less pigmentation and never scales. Probably the best time for finally deciding whether a reaction is positive or negative is 96 hours after injection.

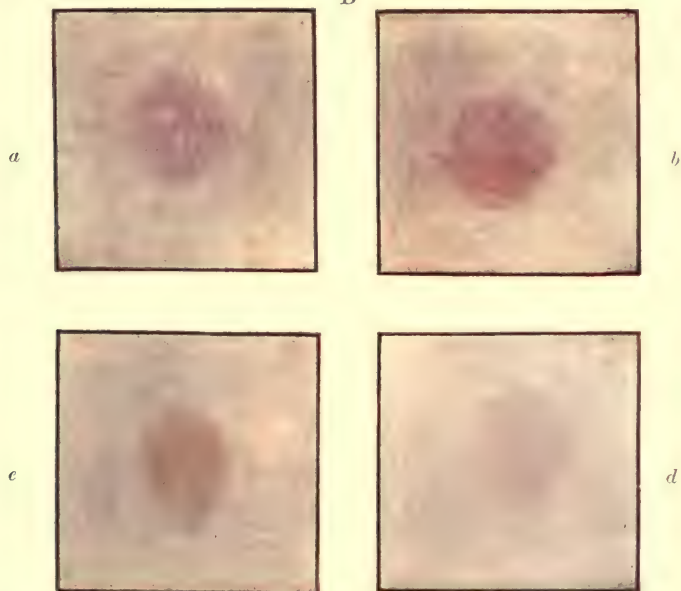
Leete has recently made a study of this reaction at the City Hospital and his results have confirmed the work of other observers. I have had the opportunity of watching the results of the test in about 1,000 cases, and it is interesting to note that the few cases of diphtheria which have arisen in hospital have all occurred in patients who had previously shown their susceptibility by giving a positive reaction. While our experience has been small I have had the advantage of examining some of our reactions, both true and false, with Dr. Abraham Zingher, whose knowledge of the practical application of the test is probably unequalled and whose advice regarding the difficulties which may arise in its working has been invaluable. I have at least seen enough of the test to be impressed with its utility. I doubt, however, if it is likely to be of much use to the practitioner. To obtain reliable data it appears to me that it should be done by one with much experience of it, and that it takes some time to acquire the necessary expertness, both in the injection and in the estimation of the result. It is important also to always work with exactly the same strength of toxin if the reactions are to be comparable. But it is to be hoped that the Schick test will be employed by skilled officials of public health and child welfare departments, and that individuals found 'positive' will be protected by immunization with the toxin-antitoxin mixture.

A



A—Shows four typical positive Schick reactions of varying degrees of intensity forty-eight hours after test; (a) is a strongly positive reaction, with vesiculation of the surface layers of the epithelium, which is seen occasionally in individuals who have practically no antitoxin; (b) and (c) are positive reactions; (d) a moderately positive reaction.

B



B—Shows a fading positive Schick reaction one to four weeks after test in various stages of scaling and pigmentation; (a) shows redness, scaling and beginning pigmentation after one week; (b) and (c) pigmentation after two and three weeks; (d) faint pigmentation after four weeks.

THE SCHICK REACTION.

(By kind permission of Dr. Abraham Zingher.)

CHAPTER XI

ERYSIPELAS

Etiology: bacteriology, predisposing causes.	Phlegmonous Erysipelas: cellulitis, erysipeloid.
Infection and Dissemination.	Complications.
Incubation.	Relapses and Second Attacks: chronic erysipelas.
Invasion Symptoms.	Morbid Anatomy.
Facial Erysipelas: the skin inflammation, the appearance, the temperature, constitutional symptoms.	Diagnosis.
Wandering Erysipelas.	Prognosis and Mortality.
Erysipelas in special situations: erysipelas of the extremities, of the genital organs, of the fauces, of the larynx, of the lungs: erysipelas neonatorum.	Treatment: general treatment, diet, drugs, serums, vaccines, local treatment.
	Prophylaxis.

Synonyms—Rose, St. Anthony's Fire. *French*, Érysipèle. *German*, Rothlauf.

ETIOLOGY. That the disease is due to a streptococcus was first proved by Fehleisen. In his opinion the micro-organism, which he successfully isolated from cases of erysipelas, possessed cultural and other characters which distinguished it from the *streptococcus pyogenes*, but at the present day it is generally held that the germs are identical. Fehleisen's contention was supported by the fact that inoculation of pure cultures in rabbits and in man was followed by erysipelatous inflammation only, and never by the formation of pus. Again, the opening of streptococcal abscesses is not known to cause erysipelas, although the skin cannot escape inoculation with the streptococcus pyogenes in the process. On the other hand, the cultural distinctions described by Fehleisen have not been observed by other workers in the same field, and most bacteriologists are of opinion that the differences, noticed clinically, in the action of the micro-organisms may be explained by variation in the virulence of the infection, in the site of the inoculation, and in the resistance of the infected subject. Under certain conditions suppuration may supervene in cases of true erysipelas, and it is not necessary to assume that this is always the result of secondary infection. That the streptococcus responsible for the disease is capable of acting differently under different conditions may be held as proved by the intimate relationship

which undoubtedly exists between erysipelas and puerperal fever. It seems beyond question that the latter has resulted when a woman has been delivered by a medical man suffering from erysipelas or in attendance upon erysipelas cases. Doctors, moreover, are said to have contracted erysipelas from women suffering from puerperal fever. Again, erysipelas neonatorum has been observed in infants whose mothers were the victims of puerperal sepsis. It is also hard to resist the conclusion that the erysipelas occasionally met with in septic cases of scarlatina is merely due to the streptococci which are always present in the nasal discharges of that disease, and which may be able, if suitably grafted by a process of auto-inoculation, to cause a typical skin inflammation.

The streptococcus pyogenes, however, is not the only form of streptococcus which is capable of producing erysipelas. A short-chained type, the *streptococcus faecalis*, first differentiated by Andrewes and Horder, was identified as the causative micro-organism in some cases of erysipelas by Panton and Adams. These observers do not regard erysipelas as, in the true sense, a specific disease, as it can be produced by a variety of organisms of the streptococcus class of which pyogenes is the most frequent example. Erysipelas and cellulitis only differ in the effects caused by acute inflammation of the superficial structures in the first case and of the deeper in the second.

The streptococcus is found in the lymphatic vessels and spaces of the corium, and is most abundant in the area just beyond the spreading edge of the dermatitis. In the parts over which the inflammation is passing, or has recently passed, it is more difficult to find, the spaces being filled with large numbers of leucocytes, and it is by no means easy to recover it from the fluid contents of the bullæ.

Before the micro-organism can obtain a nidus it is necessary that there should be a breach in the epithelium, whether this is a mere microscopic abrasion or an actual wound. It was for long customary to classify erysipelas as either *traumatic* or *idiopathic*. The latter heading covered the large class of face cases in which no wound is visible. But in such cases careful examination often reveals minute scratches or abrasions at the point from which the inflammation has spread. Even if no obvious breach in the cuticle can be detected, it may yet be present, or, indeed, may have completely healed during the period of incubation. It is both wiser and more convenient, then, to drop the old classification and to regard all erysipelas as dependent on trauma.

As regards *predisposing causes* climate appears to exercise little or no influence, the disease occurring in all parts of the world. Season is

of more importance. Most authorities agree that cold and damp weather favours the prevalence of erysipelas. Our experience in Edinburgh has been that the disease is most frequently seen in the months from October to January inclusive, a marked rise in the number of cases having occurred every October since the system of notification was introduced. During the four months named the monthly number of cases has varied little, but a sudden drop occurs in February, and thereafter there is a gradual decline to a minimum, which is reached either in June or July. I have often noticed that cold winds, or a period of cold wet weather, appear to cause an increase in the number of the relapses which occasionally occur after a patient has left hospital. It is only reasonable, therefore, to assume that such conditions favour the original attack. Chilling of the skin surface, doubtless, reduces the supply of blood to the part, and may in that manner lower the resistance.

As regards the influence of *sex*, there seems to be little doubt that erysipelas affects females somewhat more frequently than males, though a study of the sex of fatal cases would lead to exactly the opposite conclusion, the percentage mortality of males being considerably higher. Of the 1,643 cases of erysipelas seen by myself in the last fourteen years, 45·5 per cent. were males and 54·5 per cent. females. Of the fatal cases, on the other hand, 56·8 per cent. were males and 43·1 per cent. females. This series, however, excludes erysipelas of the newly born, as such cases seldom are sent to hospital. Were they included, it is probable that the percentages both of incidence and mortality for the two sexes would be considerably modified.

It has been said that persons of from thirty-five to fifty-five years of *age* are more liable to erysipelas. In my own statistics the great majority of the cases fall between the ages of 20 and 60 years, each of the first decades showing a definite increase, the maximum being in that between 40 and 50 years. A marked fall occurs in the next decade, which is still more accentuated when the age of 60 is passed. Only 2·6 per cent. of my patients in this series were over 70 years and one woman was over 80. Five octogenarians, however, figure in my records. (Table H, p. 482.)

There can be but little doubt that *alcoholism* plays some part as a predisposing cause. A very high percentage of my patients have been alcoholic. It can be readily seen that a drunken man is very liable to suffer from abrasions, and that slight injuries are often neglected and become infected. Exposure may also assist in facilitating the onset of the disease in these cases. Such causes also as poverty, overcrowding, and unhealthy conditions of life may also predispose. Broadly speaking, the erysipelas patient represents the lowest social class treated in a fever hospital.

INFECTION AND DISSEMINATION. In the days before the hygienic conditions in surgical wards reached the high level now usually observed, it was not infrequent for outbreaks of erysipelas to be associated with one or more particular beds. There was one bed in a surgical ward in the Edinburgh Royal Infirmary in which almost every operation case developed the disease, and ultimately the surgeon in charge was reduced to using the bed for cases of simple fracture. In a similar instance elsewhere it was found that erysipelas appeared in a ward when a drain outside the window was left uncovered. Modern sanitation and the better application of antiseptic surgery have between them prevented the possibility of such occurrences to-day, but the possibility of bad hygienic conditions predisposing to infection must not be overlooked.

Clean operation wounds, rather than those which are already septic, are most likely to be infected. When I first took charge of the Edinburgh City Hospital, I was much struck by the fact that though many patients, with dirty suppurating wounds, but not suffering from erysipelas, were admitted to the wards, none of them ever contracted the disease, although the conditions were all in favour of a spread of infection, the precautions taken against it being extremely primitive. This was very different to my previous experience as a house surgeon in a general hospital, where, in spite of much more attention to antisepsis, I had seen erysipelas spread to patients who had been recently operated on, and whose wounds bid fair to heal by first intention. The presence, then, of other micro-organisms in a wound may to some extent be a protection against infection.

Certain other diseases are not infrequently followed by erysipelas. Of these we may particularly note scarlatina and small-pox. Occasionally also typhoid convalescents are attacked. But, curiously enough, nothing predisposes so much to an attack of erysipelas as the fact that the patient has suffered from the disease previously. In this respect it differs from most of the other acute infections.

As regards *dissemination* the infection is carried on the hands or instruments of a surgeon or dresser. Diffusion by the air may perhaps be possible if the dust of a ward or room contains the streptococcus, but certainly plays a very insignificant part in the production of the disease. Fomites undoubtedly retain infection for some time, and an outbreak among surgical patients has been traced to the pillows of an operating table. Apart from surgical outbreaks, epidemics are rare. Erysipelas is an endemic disease, and, as we have seen, has a certain seasonal prevalence, but seldom becomes truly epidemic.

INCUBATION. The exact limits of the latent period are somewhat

doubtful, but it may be taken that from three to eight days is a probable incubation. In the cases inoculated by Fehleisen the latent stage varied from sixteen to sixty-one hours.

INVASION. The onset of erysipelas is sudden, and usually severe. The most constant symptom is *shivering*. Actual rigors frequently occur. The temperature runs up rapidly, often reaching 104° or 105° in a few hours (Fig. 51). Headache is usually complained of and may be very severe. Vomiting is common, and there is always loss of appetite and a feeling of general discomfort. Not infrequently there may be some complaint of sore throat, and I have noticed this in many cases in which there was no reason to believe that a true erysipelas of the fauces was present. There may be some swelling and tenderness of the cervical glands. These initial symptoms may precede any visible skin inflammation by a few hours. More commonly the erysipelatous flush appears synchronously with them.

FACIAL ERYSIPELAS. The period of invasion, then, is very short, the fever reaching the acme at once, and the local condition being usually well marked from the onset. In describing the stage of advance it will be well to take facial erysipelas as a type, and afterwards consider the inflammation as it affects other situations. The starting-point is usually either the inner canthus of the eye or the neighbourhood of a nostril.

An abrasion, however, on any part of the face, or on one of the ears, may be the original situation. At one of these points a patch of redness appears and rapidly spreads over the face. The affected skin becomes deep red in colour, swollen, and often shiny. It is tense to the touch and feels hot. Tenderness is well marked, especially in those parts of the skin most recently involved. The inflamed area is definitely raised above the level of the surrounding parts, and this is particularly well seen at the margin of the

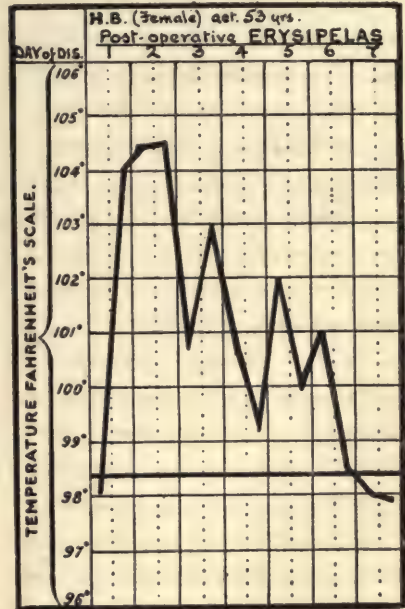


FIG. 51. A case of erysipelas from the first day, illustrating the rapid rise of the temperature. The point of infection was a nearly healed wound, the result of an operation for excision of the breast. The dermatitis involved the upper arm and the back, the spread on the former ceasing on the third day. The advance on the back continued till the seventh day, when it ceased abruptly.

advancing patch. On drawing the finger across the face from the healthy to the affected part, this margin is definitely felt as a raised ledge, the *spreading edge* of erysipelas. At this edge the colour of the inflamed skin is most vivid, gradually shading off to the point from which the dermatitis originated. The patient suffers much local discomfort, usually complaining of a burning or smarting sensation, and often of stiffness of the skin.

The rapidity with which the advance of the dermatitis takes place differs very much in different cases, and in any given instance varies with the situation which the inflammation has reached. Where the skin is lax, as in the neighbourhood of the eyelids, the spread is often extraordinarily rapid. Where it is more tensely stretched, as on the upper part of the brow, the advance of the dermatitis is much more leisurely. The resulting swelling is also best seen where the tissues are loose. The eyelids, for instance, become extremely œdematous and the eyes are nearly always completely closed. If the original lesion has been at the inner canthus of one eye, spread usually takes place across the root of the nose and the other eye becomes rapidly involved. This not infrequently causes the inflamed area to assume the outline of a pair of spectacles or, as it spreads down on the cheeks, a butterfly pattern. It has been well said that the dermatitis spreads like water on blotting-paper, small tongue-like projections shooting forward and being followed by the main line of advance.

Not only is the rapidity of the spread much influenced by the character of the subcutaneous tissues over which it passes, but the general tendency of the inflammation is to move always in the direction of least resistance. Except in the more severe cases it is common to see the advance checked altogether in places where the skin is tense, as, for instance, at the edge of the scalp, or along the line of the lower jaw. The point of the chin is almost always spared. This has been explained by the fact that the dermatitis spreads along the lines of the subcutaneous connective tissue bundles, which in this situation are vertical instead of being horizontal or oblique. In any case the skin in this situation is usually tensely stretched. In wandering erysipelas, when the whole body is liable to be affected, a similar check to the advance is presented by the skin covering the crest of the ilium, and again by Poupart's ligament.

When the inflammation is at all severe it is common for *blebs* or blisters to form on the affected surface. These are filled with a yellowish serum which, however, does not usually contain streptococci. In bad cases, if the skin is very tense, some superficial necrosis may also take place. The redness of the skin in any given situation usually remains fairly well marked for four or five days, though it gradually fades and becomes less vivid.

Desquamation, often very profuse, follows, and this may be seen in one part of the face while the disease is still fresh and spreading in another.

The patient who suffers from facial erysipelas presents a very characteristic *appearance*. The whole face is enormously swollen and deep red in colour, and the eyes are usually completely closed by the œdema. Although the disfigured features are scarcely capable of expression, the patient looks very miserable and woebegone. Should bullæ or superficial necrosis be present, the face becomes even more unattractive. The disfigurement is so complete that it is often impossible to recognize a patient with whom one may be well acquainted. The ears are much swollen and are often blistered. The tenderness of the affected skin makes it difficult for the sufferer to lay his head on the pillow without pain, and this is particularly the case if the dermatitis has invaded the scalp.

The inflammation in the vast majority of facial cases does not overstep the boundaries of the face, except in so far that the ears are frequently involved. We have seen that the tense skin of the scalp often sets a limit to the advancing margin, and that the line of the lower jaw does not seem to be easily passed. But spread may occur from the face, and, should it do so, the scalp is usually first attacked, the erysipelas reaching the trunk from thence by way of the back of the neck.

We have seen that the *temperature* at the time of onset is usually high. As the erysipelas declares itself, this high level is maintained with little or no remission. In a certain number of patients, it is true, the fever may be very moderate or, indeed, trivial, but in few acute diseases do we see such high and persistent pyrexia in adults. The fever persists as long as the

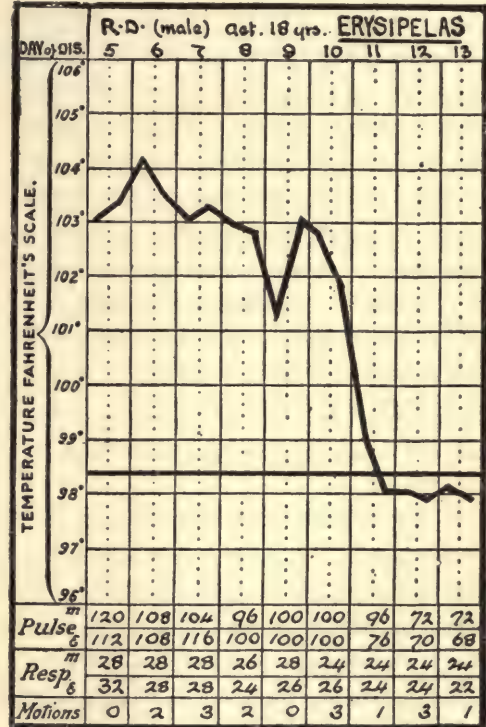


FIG. 52. A case of erysipelas limited to face and scalp. The latter was invaded on the sixth day. Note the comparatively steady temperature and the definite crisis.

dermatitis continues to advance, and varies little in character or severity even if the scalp becomes invaded. When, however, the inflammation commences to 'wander' over the rest of the body, the temperature assumes a remittent type with long morning swings towards the normal line. This change in the type of the fever is well seen in Fig. 53. If, on the other hand, the erysipelas does not spread from the face, the temperature falls abruptly with the cessation of the acute process, and the fever terminates by *crisis* (Figs. 52, 54). The fall is often very precipitate, but may in some cases last for two or three days, and occasionally evening rises are observed, as in the relapse in Fig. 54. The date at which this critical improvement occurs varies much in different cases. It may appear as early as the second, third, or fourth day of illness, or, if the scalp becomes involved as well as the face, may be delayed till after the fourteenth. Perhaps from the fifth to the tenth day is the most likely time for it, and in a recent series 62 per cent. of the cases terminated within these limits, 19 per cent. earlier and 18 per cent. later. The numbers terminating on each of the days from the 4th to the 9th inclusive were approximately equal. But the point to remember is that it may occur at almost any time, and that it is quite impossible to predict it in any given case. Failure to realize this has too often led to a sudden amelioration being attributed to the action of some particular mode of treatment.

As is only to be expected in a disease attended by so much fever, the *constitutional symptoms* are usually severe. The pulse is accelerated in proportion to the elevation of the temperature, and the respirations are correspondingly frequent. In prolonged cases congestion of the lungs, or even broncho-pneumonia, is liable to supervene. The head symptoms, however, are the most important and the most troublesome. *Headache* often persists for some days from the onset. *Insomnia* is usually an early symptom, and, if not treated promptly and successfully, may become almost intractable. It is the sleepless patients who are most liable to *delirium*, a very common manifestation in erysipelas, and one which is seldom absent even in moderately severe cases. So many of my patients are alcoholic that I find it difficult to decide how far these head symptoms depend upon toxæmia, or how far they are merely the result of alcohol, but they unquestionably occur in temperate persons. The delirium may be of the excited variety, and is in alcoholics usually of this type in the early days of the illness. The patients are very violent, constantly attempt to leave their beds, and are extremely noisy. Only too often they require mechanical restraint. If the crisis does not occur early, delirium of the low muttering type follows the period of excitement, and the patient, as his strength

becomes less, drifts into the typhoid state. Occasionally coma supervenes, and is often, but not invariably, followed by death.

Meningitis is rare in erysipelas, but it may occasionally be simulated, as is the case in typhoid and some other fevers, by meningeal symptoms depending upon toxæmia and which it is convenient to classify under the name of 'meningism'. It is generally admitted that all these cerebral symptoms are liable to be most marked and most common in cases in which the inflammation has involved the scalp.

As regards other symptoms, the *glands* in the immediate neighbourhood of the active process are usually swollen and tender, but may be expected to resolve without suppuration. The tongue is heavily furred and often very foul, and the lips and teeth may become covered with sordes. Vomiting occasionally persists for the first few days, and may be so severe as to be dangerous. Constipation is commonly present, but diarrhœa may sometimes be so marked as to assume the importance of a complication. *Albuminuria* is very frequent. The diazo reaction is sometimes present in the urine.

WANDERING ERYSIPELAS. Should the inflammation pass the limits of the scalp or face, its usual path of progress is by the back of the neck, from which it may spread forwards below the chin, and downwards on to the shoulders. The advancing margin frequently runs down the arms, and, if this extension takes place, it may stop anywhere between the shoulder and wrist. The latter situation may be reached, but it does not apparently lend itself anatomically to the spread of erysipelas, as the inflammation almost invariably stops there. Passing over the back and upper part of the trunk the dermatitis advances with varying rapidity, sometimes halting for one or two days at a time, sometimes creeping forward so slowly that the total advance in twenty-four hours may be less than an inch, and sometimes, again, covering 6 or 8 inches a day. The costal margin is often an obstacle to its progress, and in many cases the abdomen is not reached. If, however, extension takes place, the spread continues unchecked to the crest of the ilium or Poupart's ligament, which are both apt to retard the advance of the inflammatory process. Another common situation for a halt to take place is the upper part of the thigh, a little below the buttocks. But in a certain proportion of cases the erysipelas progresses with hardly a check till the feet are reached, and I have seen an erysipelatous margin run over the dorsum of the foot, involve the toes, and then, spreading over the sole, move up the back of the calf, and attack skin which it had already passed over in its progress down the body. Cases of this type may be very prolonged, lasting six weeks or even more. The spread of the inflammation is, as a rule, by continuity, but occasionally small patches of erysipelas appear

like outposts 1 or 2 inches in front of the advancing line. It is said that examination always reveals slender pink lines on the skin, uniting these outlying patches to the main body, but I have often failed to find them. Should they be visible, they no doubt indicate the lymphatic vessels by which the germs have advanced. The fever in 'wandering' erysipelas, as has already been noted, is apt to assume a remittent type. The chart of a typical case, in which the inflammation reached the thighs, is shown in Fig. 53. The disease is a very exhausting one, and death may occur before

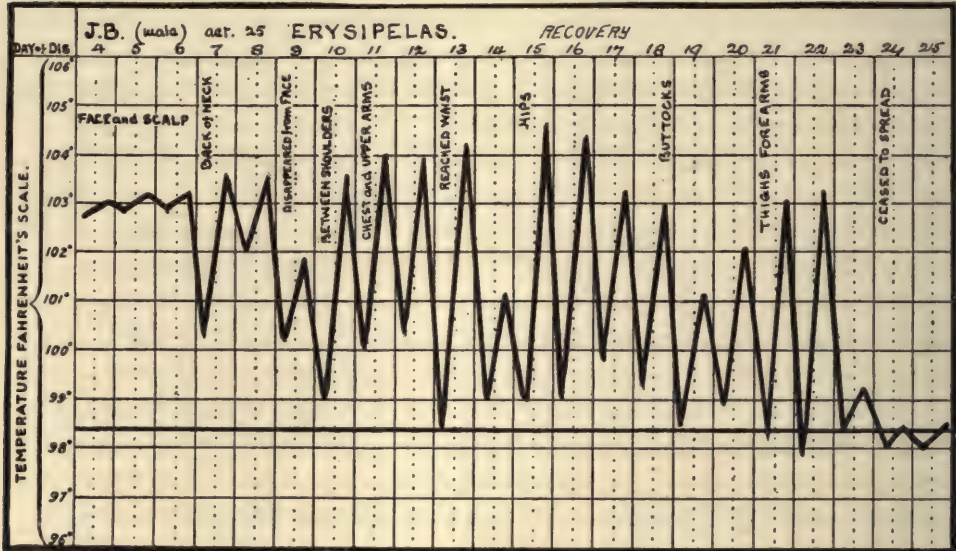


FIG. 53. A case of 'wandering' erysipelas. Note the 'continued' type of fever while disease is limited to face and scalp and the subsequent 'remittent' type as the body is invaded. Recovery.

the erysipelas shows any signs of stopping its advance. The patient is often much wasted. In these cases the gradations in the intensity of the dermatitis, from the spreading edge backward to the skin areas which are desquamating or have regained the normal appearance, are very well marked. In my series the type has not been very common, erysipelas wandering from the head, or from the extremities, in somewhat less than 7 per cent. of the whole.

ERYSIPELAS IN SPECIAL SITUATIONS. The **scalp** is frequently affected. This may be as the result of spread from the face, but often the origin of the inflammation is a scalp wound. In the latter event the face seldom escapes, erysipelas spreading much more readily from the scalp than to it. The general symptoms of the disease are the same as in a face case,

but the spreading margin is best defined by the limits of tenderness on pressure, it being difficult to either see or feel the actual edge. The head symptoms are always severe and the headache very intense. The hair falls out in large quantities in convalescence. When a scalp wound is present deep suppuration is comparatively common, and there is much burrowing of pus under the integument.

The **extremities** may be the original site of the lesion, the legs being much more frequently attacked than the arms. In the cases which have come under my notice a varicose ulcer on the leg has been very often the point of origin. Phlegmonous inflammations are common and suppuration occurs frequently. A whole limb is often involved and the erysipelas occasionally may wander on to the trunk. The extremities were primarily attacked in about 13 per cent. of my 1,643 cases.

The **genital organs** in the male may be the starting-point of an erysipelas, or may become involved in a general spread of the inflammation over the body. A circumcision wound may be the primary site. The lax tissues of the scrotum become extremely œdematous and sometimes very tense. Extension usually takes place on to the thighs, and the trunk may also be attacked. In young children the risk of excoriation and superficial necrosis of the skin of the scrotum is very great. In women the disease may originate on the vulva, or apparently even in the vagina itself. Such infection is usually the result of a puerperal sepsis. The labia become much swollen and extremely painful, and the usual constitutional symptoms of erysipelas are present. Extension may take place outwards over the thighs and buttocks, and cases have also been reported in which the inflammation has spread internally and, involving the uterus and tubes, caused fatal peritonitis. Such a condition, however, has never come under my own notice.

The **fauces**, as we have seen, may be painful in cases of ordinary facial erysipelas. Occasionally the inflammatory process is originally located in this situation, or again, extension may take place from the face by way of the mucous membranes of the mouth. Neither primary or secondary faucial erysipelas has been as common in my experience as it would seem to be in that of others. Possibly the great attention paid in all our fever cases to the antiseptic toilet of the mouth has reduced the probability of extension of the inflammation from the face. When the mucous membranes of the mouth and throat are involved there is much œdema and the fauces become an extremely dark red in colour. The mucous membrane looks tense and shiny, and the uvula is much enlarged. Occasionally superficial ulcerations, apparently the result of ruptured bullæ, are observed. Swallowing is extremely difficult, and pain is a very prominent symptom. If the whole

mouth is involved the tongue is oedematous, and there is much salivation. The inflammation, if its primary focus is in the fauces, may spread to the face by way of the nose, emerging either at one of the nostrils, or by the nasal duct to the canthus of the eye. Or less frequently it may appear at the corner of the mouth. Rare cases have been reported in which extension took place by the Eustachian tube, and erysipelas appeared at the external auditory meatus. When the *nose* is involved in the process the affected nostril may be blocked. Sometimes there is considerable coryza.

It has been suggested that certain unexplained cases of oedema glottidis may be due to a primary erysipelas lesion in the **larynx**. This is, of course, perfectly possible, but, unless the erysipelas spread upwards and ultimately involved the face, it would be practically impossible to make a certain diagnosis of such a condition. The main symptoms of laryngeal erysipelas are said to be pain on swallowing, tenderness over the larynx, and ultimately acute dyspnoea. Profuse expectoration of clear fluid has also been observed. Judging from my own experience, the condition, whether primary or secondary to faucial erysipelas, must be extremely rare. Although I do not possess records of all the cases which have passed through my hands in the last twenty-three years, I can say with some certainty that I have only once seen laryngeal obstruction develop in erysipelas, and at a moderate estimate my experience must cover 3,000 patients. The single case was one of oedema glottidis occurring in an infant of two weeks old, originally infected in the skin of the scrotum. A certain amount of hoarseness, on the other hand, has been not uncommon in faucial cases.

Erysipelas of the **lungs** has also been described. The inflammation is said to be of a wandering variety, successively involving different areas. Secondary pneumonia is not uncommon, and may well, in some cases, be due to streptococcal infection. But unless facial erysipelas immediately followed the appearance of the pulmonary symptoms the diagnosis of a primary focus in the lung would be quite unjustifiable.

Newly-born infants may be attacked by erysipelas, infection taking place at the navel or in its neighbourhood. This form of the disease, **erysipelas neonatorum**, does not present essential differences from the ordinary variety. The spreading margin, however, is often not very distinctly raised. The erysipelatous blush usually originates in the hypogastrium rather than at the navel itself, and may be the result of puerperal septicæmia occurring in the mother, or merely of accidental streptococcal infection of the umbilical wound. The inflammation is often of the wandering variety, and the genital organs and buttocks are frequently involved. Superficial necrosis or extensive sloughing of the whole of the skin tissues may supervene. The fever

is often considerable, and remittent in character. The condition usually appears within a fortnight of birth, and is very frequently fatal. Death may occur with comparative suddenness, sometimes within one or two days of the onset, sometimes as the result of a prolonged attack and after much sloughing of the skin.

Modern aseptic precautions have made **vaccination erysipelas** extremely rare. I have seen very few instances of this unfortunate occurrence, and without exception they have been the result of a late infection of a neglected sore. The tender age of the patient makes the condition a serious one.

PHLEGMONOUS ERYSIPELAS. The inflammation is said to be phlegmonous when the deeper structures are involved. Such involvement of the cellular tissue may be regarded rather as a complication than as a manifestation of true erysipelas, but it is not infrequently seen in the neighbourhood of dirty wounds, such as varicose ulcers, which have been the starting-point of a genuine attack. Watson Cheyne regards it as the result of mixed infection, but if we regard the streptococcus pyogenes as the cause of erysipelas, it is reasonable enough to suppose that the same micro-organism is responsible for the cellulitis. In these cases there is much more resistance to the touch and less elasticity than in the more superficial inflammation. Suppuration often occurs, and even after energetic surgical intervention there may be difficulty in checking the burrowing of the pus, abscesses sometimes occurring at quite unlooked-for points. The cellular tissue may slough extensively, and, till the sloughs are removed, there is no chance of the suppuration ceasing. The cellulitis often keeps pace with the spread of the erysipelas, and a whole limb may be involved. In some cases incisions made to relieve tension fail to find any pus, and there may be much superficial necrosis. Erysipelas complicated by this phlegmonous inflammation is very dangerous, especially in the aged. It may be months before all the sinuses are closed, and the patient often becomes much exhausted, and may die in the 'typhoid state'. Occasionally in very severe cases amputation of a limb may become necessary, as the result of definite gangrene.

A condition closely resembling erysipelas has been described by Rosenbach, Lenhartz, and others under the name of *erysipeloid*. I have been on the look-out for this for several years, but hitherto have been unable to identify it. As described, it most commonly affects the fingers of persons whose occupation brings them into contact with meat, fish, and poultry. A slowly spreading inflammation of a dark red colour, and with a definitely raised margin, moves upwards from the tip of the finger. There is no fever or other constitutional symptom, and the dermatitis subsides in about

a week. The face may also be attacked by this condition, and Lenhartz is inclined to regard those facial cases without temperature, which present a butterfly pattern of the inflammation on the face, as being in reality instances of erysipeloid. Cases answering this description are occasionally admitted to hospital, but do not present sufficient distinction from erysipelas to be regarded clinically as another disease. Bacteriologically erysipeloid is said to depend on infection by a coccus distinct from the streptococcus, but the researches regarding this organism were carried out more than thirty years ago, and, considering the difficulties of the whole question, need confirmation.

In rare instances, instead of the affected skin becoming brilliantly red, it remains almost white. This condition, the *érysipèle blanc* of the French physicians, I have only seen on one occasion, in a woman who was the subject of very profound anæmia. Her bloodlessness probably accounted for the absence of the erysipelatus flush, but there was no doubt as to the margin.

COMPLICATIONS. Of these the most frequent is probably *broncho-pneumonia*. This has been attributed to streptococcal infection. It is most often observed in the wandering variety of the disease, and adds much to the danger of the case. Bronchitis is also occasionally met with. A few instances of acute *nephritis* have come under my notice. *Meningitis* undoubtedly occurs, but is extremely rare. By many, *cellulitis* is regarded as depending on a mixed infection, and is therefore classed as a complication. *Abscesses* are common in facial erysipelas, and are often seen in the lower eyelids. In prolonged cases *pyæmia*, with abscesses in various parts of the body, is sometimes observed. As mentioned above, *diarrhœa* may be very intractable and sometimes determines a fatal result. The literature contains references to a very few instances of myelitis and paraplegia.

RELAPSES AND SECOND ATTACKS. The immunity conferred by an attack of erysipelas is extremely short-lived. Indeed, a person who has once suffered from the disease is much more liable to it than he was before his original illness. **Relapses**, occurring at any time from a few days to six weeks after an attack, are relatively frequent. In hospital they have been attributed to infection from another acute case admitted to the ward during the convalescence of the patient. But it is more reasonable to regard them as instances of auto-infection, micro-organisms, which have remained latent at the site of the original abrasion, having become active as the result of some irritation, often unexplained, and causing a repetition of the inflammatory process. All the symptoms of the original fever are reproduced. Sometimes the relapse is even more severe than the first attack, more often it is

shorter in duration and more moderate in intensity. An illustration of the temperature in a case of relapse is given in Fig. 54. Occasionally two or three relapses may follow each other at short intervals. In women their appearance may correspond with the menstrual periods. In a series of 386 cases, 28, or nearly 7 per cent., of the patients relapsed, and two individuals had no less than three distinct relapses before leaving hospital. In my more recent series, however, of 1,643 cases relapses only occurred in 4 per cent.

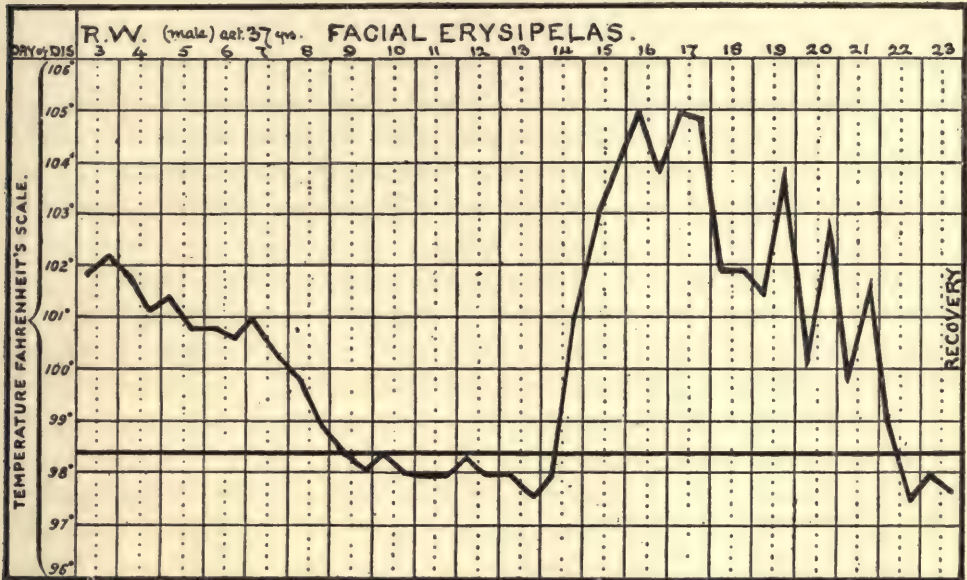


FIG. 54. Showing temperature of a facial case, followed by relapse. In both attacks the termination of the fever is comparatively abrupt. The high levels so frequently observed in erysipelas are well illustrated in the relapse. The face alone was affected on each occasion.

Second attacks, that is to say, repetitions of the disease after a long interval, are even more common. In the first series, 17 per cent. of the patients had suffered previously from erysipelas. Of these, seventeen, or more than 4 per cent. of the whole, had had three or more previous attacks. In the second series previous attacks were noted as having occurred in 11 per cent. The disease is particularly liable to recur in persons who have a habit of picking the nose or scratching the eyelids. It is usual for the recurrent attacks to originate in the same situation. Sometimes erysipelas attacks the same individual annually, appearing with some suggestion of regularity in the spring. It is by no means the rule for these repeated manifestations of the disease to be trivial in their nature. Often, it is true, they are so, but

I remember losing one patient, whose frequent visits to the hospital had made him almost an old friend, in his seventh attack.

Occasionally the inflammation remains present in a subacute form for such long periods as to justify the name of *chronic erysipelas*. I once had a patient under my care who for over six months suffered from facial erysipelas which, varying much in intensity and sometimes almost disappearing, never entirely left her during that period. The skin of the face became much thickened, and a definite margin was usually, though not always, to be felt. The patient's attack was at first quite acute and of an ordinary nature. The temperature, however, soon subsided, and, except for occasional exacerbations, remained normal. On the other hand, the inflammatory condition never entirely disappeared, and the case could hardly be regarded as one of repeated relapses. The patient was in the habit of picking her nose, and it was found necessary to control her hands before any permanent improvement could be obtained.

MORBID ANATOMY. The inflamed area loses its red colour after death, but some degree of œdema may remain in the lax tissues and there may be desquamation visible in those parts over which the dermatitis has passed. The viscera present no special features of interest beyond the microscopical appearance suggestive of fever and toxæmia. Occasionally pyæmic abscesses are present.

DIAGNOSIS. As a rule there is but little difficulty in recognizing a case of erysipelas. The great feature which distinguishes it from any other skin condition which may have a superficial resemblance to it is the definitely raised margin. Whereas other inflammations are most intense at their centre of origin, and fade off towards the periphery, that of erysipelas presents an exactly opposite condition, the greatest intensity of colour, the most marked tenderness, and the most obvious œdema, except when such structures as the eyelids are involved, being all seen in the neighbourhood of the spreading edge. The parts nearer the origin of the dermatitis, on the other hand, are less actively inflamed, and may already present evidence of desquamation. In doubtful cases the presence of definite bullæ or vesicles affords a strong argument in favour of a positive diagnosis. It may be also noted that in swelling of the face from other causes, such as an alveolar abscess or a parotitis, the ears remain normal, whereas in erysipelas, should the œdema extend to that situation, the inflammatory process almost always involves the ears, which become extremely œdematous and painful. The marked constitutional symptoms, moreover, which accompany the onset of erysipelas, will serve to distinguish it from most of the conditions with which it may be confused.

Simple *erythema*, especially, is likely to be unaccompanied by constitutional symptoms. There is no tenderness on pressure, and no complaint of tenseness or pain. The margin is usually ill defined and is not definitely raised. The face may be puffy, especially round the eyes, but frequently this puffiness is not associated with redness and, indeed, may be quite independent of the erythematous patch. The erythema itself is often blotchy and not so uniform in appearance as the erysipelatous blush. I have occasionally seen *erythema nodosum* intimated as erysipelas. In these cases it is a raised tender and inflamed area, usually on the legs, which has led to the mistake being made, but it is unusual to find only one patch, and the multiple character of the condition should make its real nature quite clear. The distinction between erysipelas and diffuse *cellulitis* is much more troublesome, especially as the latter may occur as a complication of the former. The fact, moreover, that the streptococcus pyogenes may cause both conditions suggests that in some cases the inflammation may be, as it were, on the border-line between them. But the absence of any well-defined margin, and the fact that the tenderness is not more marked at the periphery than at the centre, should be against a diagnosis of erysipelas. The colour of the skin in cellulitis is not so brilliant. It is usually darker and more inclined to purplish tints. The more brawny swelling and greater resistance of cellulitis must also be remembered. In simple *lymphangitis* the redness is more diffuse and the darker lines of the lymphatic vessels are often prominent.

I cannot say that I have any confidence in my ability to recognize an erysipelas of the fauces, although many have described this form of sore throat as characteristic. Marked swelling and cedema and very intense pain are the characteristic features, and there is a tendency to the formation of small vesicles which may leave a sloughing surface after their rupture. But severe throats in scarlatina may have all these characteristics, and it is safer to wait for a skin surface to be involved before assuming a throat inflammation is erysipelatous.

It is not necessary to do more than mention the other conditions which have been mistaken for erysipelas. Such inflammations as eczema rubrum, pemphigus, herpes, and malignant pustule should not cause much difficulty in diagnosis.

PROGNOSIS AND MORTALITY. Of the 3,885 cases of erysipelas intimated in the first thirteen years of compulsory notification in Edinburgh, 188, or 4·8 per cent., died, and this may probably be regarded as an average rate of mortality for persons of all ages. The hospital mortality has been slightly higher, the last series of 1,643 patients showing a rate of 5·7 per

cent. This difference is perhaps accounted for by the fact that the most fatal type of case, the alcoholic, is seldom treated at home. The chances of recovery are certainly influenced by the *age* of the patient. Erysipelas is extremely fatal in the newly born, and the mortality, as will be seen in the table, is high up to the age of 5 years, and considerable up to 10 years. The fewest deaths occur in the decade from 10 to 20 years and thereafter the fatality rate increases steadily with age until a figure of over 25 per cent. is reached for patients above the age of seventy. The most frequent causes of death in old age are myocardial changes, general sepsis, and surgical complications. Schlesinger has reported a mortality of 25 per cent. in a series of 224 patients of over 60 years, which suggests that my own figures may considerably understate the risks.

TABLE H

Age Periods.	Males.			Females.			All Cases.		
	Cases.	Deaths.	Per cent.	Cases.	Deaths.	Per cent.	Cases.	Deaths.	Per cent.
0-5	46	7	15.2	32	2	6.0	78	9	11.5
5-10	21	1	4.7	29	1	3.4	50	2	4.0
10-20	72	2	2.7	114	1	0.8	186	3	1.6
20-30	119	2	1.6	153	4	2.6	272	6	2.2
30-40	130	4	3.0	166	7	4.2	296	11	3.7
40-50	160	9	5.6	185	7	3.7	345	16	4.6
50-60	107	13	12.1	128	10	7.8	235	23	9.7
60-70	71	9	12.6	66	5	7.5	137	14	10.2
70-	21	7	33.3	23	4	17.3	44	11	25.0
Totals	747	54	6.9	896	41	4.5	1,643	95	5.7

Table H. Showing age distribution and mortality according to age and sex in 1,643 consecutive cases of erysipelas.

As regards *sex* females appear to have a considerably better chance of recovery than males, particularly after the age of forty is passed, although the table also shows that under the age of twenty years males seem to suffer most. The number of cases in the series is too small to give accurate results, and I am inclined to think that females have the advantage at all ages.

It may be broadly stated, then, that, except in the very young and the aged, the prognosis in erysipelas is most favourable. The disease tends naturally to recovery and, unless certain complications are present, a hopeful view may be taken of cases in which the symptoms appear extremely grave. The most important complication is unquestionably *alcoholism*. Were it not for that, I hold that the mortality in erysipelas would be most trivial. The alcoholic subject certainly appears to have but little

resistance to erysipelas. The fever is high, the head symptoms are severe, and the insomnia intractable and persistent. Pneumonic complications, also, may be looked for in these cases, and if there is any suspicion of a patient being alcoholic a very cautious prognosis must be given. Again, *chronic renal disease* is an awkward complication with which to start an attack of erysipelas. Such cases are very frequently fatal. Erysipelas, again, which appears as a complication in such diseases as scarlatina or small-pox, is often very severe, although as regards the first-named disease the contrary has been stated. It may be assumed that surgical erysipelas, that is to say, erysipelas following an operation, is more dangerous to life than the so-called idiopathic type. The weak state of the patient, the extent of the infected wound, and the probability of exhausting suppurative complications, all tend to increase the risks.

As regards the symptoms presented by the patient himself, too much attention need not be paid to high levels of pyrexia, even if there is little or no remission in the course of the fever. Often patients with temperatures ranging from 104° to 106° make excellent recoveries, and provided the pulse is satisfactory the prognosis may be quite favourable. The pulse, in fact, is a much more trustworthy guide. The worst cases are those in which the inflammation spreads to the scalp, the constitutional symptoms being often very severe and delirium an almost constant feature. Such a complication as pneumonia adds very considerably to the gravity of the outlook. In cases of 'wandering erysipelas' death may occur from exhaustion, and in this form of the disease even a moderate amount of diarrhoea may seriously compromise the chances of recovery. Albuminuria is present so often that, unless the amount of albumen is very considerable, it may be disregarded so far as prognosis is concerned. The symptom of most evil omen is wild delirium, when the patient cannot be got to sleep and is constantly fighting to get out of bed. Unless by appropriate treatment sleep is procured, or a satisfactory defervescence occurs early, it is rare for these cases to recover. It is, of course, obvious that the secondary involvement of the fauces in a case primarily facial adds much to the risk, and implication of the larynx is extremely dangerous.

So far as my experience goes it is quite impossible to predict how far the dermatitis will spread, or how long the fever will continue. Some writers regard the average length of a case as being about ten days, but a crisis may occur as early as the third day, or may be postponed almost indefinitely. Even when the spreading margin ceases to move forward for one or two days, there is no assurance that the advance will not be again resumed. On the other hand, as has been seen above, there are certain

situations in which spread is much retarded, and it is always reasonable to hope that they will not be overstepped by the dermatitis, though it may be safer not to give a definite opinion on this point.

TREATMENT. While we have it on the authority of no less a distinguished clinician than Trousseau that expectant treatment offers most advantages, there are few diseases for which a greater number of general and local remedies have been recommended. Many of these, as will be seen, we are justified in regarding with some scepticism, and we may follow the great Frenchman in believing that the patient gets better in spite of them rather than because of them. It is extremely difficult to estimate the value of any particular mode of treatment in a disease like erysipelas, which is so uncertain in its duration. The crisis often occurs a day or two after any form of systematic treatment has commenced. Erdman reports that in a series of 500 facial cases it occurred on an average on the sixth day. It is forgotten that when a patient is left practically untreated, improvement is often noticed equally early. What, however, can be asserted with some confidence is that all the systems of treatment advocated frequently fail to check the advance of the dermatitis, so frequently, indeed, as to justify us doubting whether they exert any favourable influence at all.

It is, on the other hand, obvious that both constitutional and local treatment is often absolutely necessary, and it will be convenient therefore to briefly note the lines on which a case may be advantageously treated, and also some of the remedies which have been most frequently employed.

General Treatment. The *diet* is of considerable importance. The main indication is undoubtedly to feed liberally. In the early stages the high fever, and occasionally the sore throat, may make a fluid diet a necessity, but as a general rule soft solids such as milk puddings, jellies, and thick soups may be used to supplement the milk and beef-tea. If there is no tendency to vomiting and the digestion is fair, there is little objection to giving solids in the febrile stage, and white fish, or even a little chicken, is often well taken, especially in 'wandering' cases with intermittent temperatures. It is in this class of case, which is so prone to dangerous asthenia, that liberal feeding is especially important. Elderly persons and alcoholics will require stimulants, but young and healthy adults can usually be trusted to pull through their illness without them. When only a small amount of alcohol is required it is best given in the form of brandy made up in egg-flip. A rapid pulse, exceeding 120, or a pneumonic complication as evidenced by accelerated respirations, may be regarded as indications for stimulation, but in all cases the result of the first few doses should be

carefully watched, and if such unsatisfactory symptoms as sweating, increased restlessness, or a more rapid pulse are noted, the alcohol should be at once withdrawn.

It is almost unnecessary to say that the patient must be kept in bed till the temperature has been completely normal for two or three days at least. It is, in my experience, of no advantage to interfere with the course of the *temperature*, even when levels of 105° or more are reached. The most that can be advised is the use of tepid or cold sponges, which make the patient more comfortable. I sometimes employ the ice-cap, but usually more to combat the *headache*, delirium, or restlessness of a patient than to secure the reduction of his pyrexia. In headache, especially, ice to the head may give more relief than anything else. It is most important for the patient to have an adequate amount of sleep, *insomnia*, if at all persistent, being a most dangerous symptom. It is well to start hypnotics early, and my present rule is to give some sedative drug at once to any patient who on admission appears likely to be alcoholic, without waiting to see if he can do without it. *Insomnia*, if left untreated too long, becomes quite intractable, and it is wisest not to let the patient get out of hand. One night's good sleep often prevents any further trouble. I have had most success with sulphonal, given in 25-grain doses at about five o'clock in the afternoon. This often acts well about four hours later, and, if not, a moderate dose of paraldehyde, say a drachm and a half or two drachms, will frequently send the patient over. But once hypnotics are started they must be pushed till the patient is asleep, or his last state is worse than his first. The great advantage of sulphonal in these cases is, that even when the results at night have been disappointing, there is much less restlessness on the following day, and the patient is relatively tractable and less likely to get out of bed. In very wild and excited cases a hypodermic injection of hyosine or morphia may be absolutely necessary, and will sometimes be effectual. For a failing heart digitalis, strophanthus, and similar drugs may be employed, but, as in so many of the other acute fevers, their action is often extremely disappointing. Strychnine, as a general rule, appears a more satisfactory drug to employ, and its tonic effect is valuable in prolonged cases. Camphor, also, will be found useful on occasion.

Certain drugs have enjoyed the reputation of being almost *specifics* in the systematic treatment of erysipelas. Of these perhaps the most widely used is the tincture of the perchloride of iron. Given in doses of 30 minims every four hours it is supposed to exert a favourable influence on the course of the disease. No doubt in prolonged cases of wandering erysipelas its tonic properties may be of value, but, though it was for long

systematically used at the Edinburgh City Hospital, I never saw any advantage result from its employment, nor did the patients fare any worse when other methods of treatment were tried. My chief objection to it is that it is very liable to upset the stomach in cases in which feeding may be all important. Very much the same may be said of quinine, which for some time had a certain vogue. Its use will no doubt commend itself to those who regard every slight reduction of temperature as a sign of marked improvement, but my experience has been that it neither cuts short the fever nor checks the spread of the dermatitis. The salicylates are in my view equally useless. I gave them a fair trial only to discard them, and some years ago tried them again in the form of salicylate of iron with equally discouraging results.

Serum Treatment. It is only natural that attempts to treat erysipelas with anti-streptococcal serum should have been made, and several writers have claimed to have obtained considerable success with the serum prepared by Marmorek. But it was soon found that the evidence regarding the efficacy of the serum was most conflicting. Enthusiasts asserted that the swelling and redness rapidly became less, that the spread and the fever were checked in two or three days, and that the desquamation occurred more early. On the other hand, it was maintained that the serum often failed to check the advance of the dermatitis, and that the sequelæ were sometimes unduly severe, so much so, in fact, that it was unwise to employ this method of treatment at all. Without laying too much stress on this last point, I think it is beyond all question that the serum has little or no effect in arresting the progress of the advancing margin. In the limited number of cases which I have treated with this serum, certainly not more than thirty in all, the dermatitis continued to advance, the high fever was maintained, and the constitutional symptoms remained equally severe for several days after the injections were commenced, and in one or two patients the erysipelas wandered over the whole body, in spite of repeated doses. The general impression then obtained was that several of the cases were the worse rather than the better for the treatment. In my opinion a serum can be of little value if marked spread of the local lesion takes place after one or two adequate doses. It is very rare, for instance, to see an extension of a diphtheritic membrane after the administration of antitoxin. On the contrary, we confidently expect to see its advance limited at once. Judging by this standard, anti-streptococcal serum is of little value, spread of the dermatitis being frequently well marked for many days after its employment. Some years ago I gave a trial to a polyvalent streptococcal serum, in about 20 cases, but the results were absolutely similar, the advance

of the margin being apparently quite unmodified by its use. As regards dosage, from 20 to 50 cubic centimetres should be given at frequent intervals, say three or four times in the twenty-four hours. It may be added that experiments in inoculating erysipelas have proved successful, even after prophylactic doses of Marmorek's serum. This, in itself, casts considerable doubt on its therapeutic value.

Welz has claimed that the polyvalent serum of Ruppel, given intravenously in doses of 100 c.c., has given him good results. He admits, however, that collapse occasionally follows the introduction of such large doses, and it seems doubtful if his success has been sufficiently marked to encourage imitators. Schlesinger found serum useless.

Vaccine Treatment. I have not employed vaccines therapeutically for erysipelas, but Erdman, whose extensive experience in the Bellevue Hospital, New York, makes his opinion particularly valuable, reports that neither vaccine therapy in a series of 95 cases, nor treatment with phylacogens in 20 others, was of any avail in ameliorating the symptoms, shortening the illness, lessening the mortality, or preventing recurrence. Others, however, report more favourably, and Sill has obtained good results in infants. His series of cases is a short one, only ten in number, but only one of these was fatal, and his oldest patient was aged only seventeen months. When we consider the high mortality of erysipelas in the very young it must be admitted that the treatment seems to have been unusually successful. Sill's usual dose appears to be 80 million streptococci followed by 120 millions on successive days. He treated an infant of 8 days with a first dose of 40 millions, and 80 millions were given on the two following days, with the result that the patient recovered. It will be remarked that the doses employed are relatively large for a streptococcal vaccine. Fischer also speaks favourably of the use of vaccines, and Takaki finds autogenous cultures satisfactory. In Edinburgh my friend Dr. Robert Robertson tells me he has been very successful in shortening the duration, and modifying the severity, of the illness by the use of mixed streptococcal and staphylococcal *sensitized vaccines*. Some of the cases treated by Sill were given a similar mixture of organisms, and it is possible that the addition of the staphylococcus may increase resistance, and in the case of cellulitis, where there may be mixed infection, might well have a specific action.

It is certainly desirable that more work on the therapeutic use of vaccines should be undertaken, but, as is the case with other forms of treatment, a very long series of cases, adequately controlled, will be necessary to establish their efficacy in a disease so variable in its duration and severity. The

method would certainly appear a suitable one for cases in which the erysipelas shows signs of 'wandering'.

Local Treatment. The object of local treatment is twofold. Firstly, it is necessary to allay the pain and discomfort suffered by the patient. Secondly, it is obviously desirable to check the spread of the inflammation, if by any means that is possible. For the comfort of the patient various lotions, unguents, and dusting powders have been employed with more or less success. The *lotions* may be applied to the face, or to the affected part, on a mask of lint, which should be kept frequently moistened. Lead lotion is often used for this purpose. Should the pain and tension be extremely severe, hot fomentations, sprinkled with laudanum, sometimes give some comfort. A lotion of ichthyol in aqueous solution, of the strength of 1-10, often gives much relief, and at one time I preferred this drug to any other, though I usually used it in the form of a 10 per cent. ointment, and considered it the best palliative in erysipelas. Since 1911, however, my routine treatment has been the application of lint soaked in a saturated solution of magnesium sulphate, as recommended by Tucker. The soaks should be covered with oiled silk or some waterproof material and kept as wet as possible. They are even more comforting than ichthyol to the patient and are much cleaner to use. The heat, redness, and swelling are rapidly reduced, but I cannot assert that the spread of the dermatitis is in any way checked. An advantage of this treatment is that Epsom salts are always readily procurable even in small villages. It may be added that cellulitis is also very favourably affected by this application, which will be found very useful in phlegmonous cases.

Ointments will be found to be at least as comforting as most lotions, and they have the advantage of requiring less attention, that is to say, they have not to be renewed so frequently. They may be either smeared over the part and left uncovered, or applied on a lint mask. The nature of the ointment is of little importance, the resulting comfort being probably due to the greasiness of the preparation. Simple vaseline is quite good enough for the purpose, but, as an antiseptic action may be desired, boracic ointment may be employed, or the ichthyol ointment mentioned above.

It is, however, often convenient to use *dusting powders*. Subnitrate of bismuth, boracic acid, and simple starch powder, used either singly or combined in different proportions, are quite suitable preparations. When nothing else is available, flour, dredged over the part, may give considerable relief and allay the sense of heat and discomfort.

Some prefer to restrict their treatment to excluding the air by the application of cotton-wool, which may be cut as a mask. I hardly regard this

as necessary if powders or ointments are used, as it makes the patient uncomfortably hot about the head. It is questionable, moreover, if the exclusion of air of itself does any good.

With the object of *limiting the spread of the dermatitis* various means, mechanical and medicinal, have been employed. We have already noted that the margin of erysipelas is often checked in its advance at points where the skin is tightly stretched over subjacent structures. To produce artificial barriers to the progress of the inflammation, strips of *plaster* have been applied to the skin just clear of the erysipelatous margin, and it has been asserted that by this method good results have been obtained. No doubt the dermatitis in many cases does halt at the barrier, but it crosses it so often that we cannot reasonably regard the plaster as the cause of the check, when it occurs. Adhesive plaster, again, is not very easy to arrange suitably on the face, and it is a positive nuisance if the dermatitis is spreading towards the scalp, or if the patient's skin is very hirsute. Painting with *collodion* round the advancing edge has also been recommended. While not having the objection to the use of collodion in erysipelas which has been expressed by Watson Cheyne, I must confess that I never saw the spread of the inflammation checked by this means, and I see no advantage whatever in its use. Another method which also acts purely mechanically is the employment of bandages applied fairly tightly round the parts expected to be next involved. I do not recollect ever having tried this plan, but my frequent failures to check the advance of erysipelas by plaster, employed as a constricting band, do not lead me to believe that it can be efficacious.

More drastic are the attempts to create an effective barrier by making *incisions* into the skin beyond the affected area and rubbing various antiseptic substances into the wounds. Kraske suggested scarifications of about half an inch in length, which were afterwards to be sprayed with a solution of carbolic acid, 1 in 20, from a steam spray producer. Others made longer incisions and preferred to dress with perchloride of mercury, 1 in 1,000 solution. To carry out such methods of treatment satisfactorily a general anæsthetic is required, surely a most undesirable thing when we remember how many of the most serious cases are alcoholic. The risk of leaving permanent scars, moreover, debars us from seriously considering this line of treatment in face cases, and, as we have seen, in nearly 80 per cent. of the whole the dermatitis is limited entirely to the face and scalp, and in about 6 per cent. more it originates in that situation. I have no right to speak as to the merits of a treatment which I have not ventured to try, but I think that simpler procedures are much to be preferred. The

injection of 1 in 40 carbolic solution in small quantities just free of the spreading margin has been highly recommended.

Perhaps the most popular of all the modes of local treatment is the application of various *medicinal substances* either on the inflamed area, or just clear of it, with a view of checking its advance. Thus broad bands of silver nitrate have been made on the healthy skin and it has been claimed that the inflammatory process is arrested thereby. Again, *iodine* has been painted on the inflamed parts and also beyond them. The preparation of iodine must be a strong one, the liniment being the most suitable, but, as a matter of fact, neither it nor the nitrate of silver is of the slightest use. I have seen patients suffering from 'wandering erysipelas' painted with band after band of iodine, until they were ring-straked like a zebra from head to foot, and have observed the dermatitis advance, practically unchecked, overstepping ring after ring. I often use the treatment for the purpose of demonstrating to students how ineffacious it usually is. If the margin stops advancing, it will frequently be found to have done so before it is near the painted band. Even if it stops in the middle of the band itself, there is no proof it would not have done so in any case. There is, however, a more or less scientific basis for these attempts at checking the spread of erysipelas, as unquestionably a local leucocytosis is set up by these substances, and we have already noted that leucocytes are found in large numbers just at, or behind, the advancing margin. Anything that would cause a large number of leucocytes to collect in the tissues just in front of the spreading edge should theoretically limit the activity of the numerous streptococci usually found in that area. To secure such a result even blistering fluid has been used as an obstructing band. Even this, however, is often passed, and when that occurs, as I have seen on more than one occasion, the last state of the patient is worse than his first.

Of other substances the application of which is supposed to exert a beneficial action on the inflammation and to limit its advance, perchloride of mercury (1-1,000 solution), resorcin, and iodide of starch may be mentioned. I have tried them all with no beneficial result. Ichthyol, though it has, as we have seen, a marked soothing influence, is powerless to check the spread of the dermatitis, even when made up with collodion, in a solution of 1 in 8, which might be expected to combine a mechanical with an antiseptic action. I have not yet tried the 1 in 1,000 picric acid solution, made up with 12 grammes of alcohol to the litre as recommended by Critzman, or the 5 per cent. solution of methylene blue employed by Nobécourt.

From the above it is clear that we cannot, in the present state of our knowledge, expect to check the advance of erysipelas, either by internal remedies or by external applications. Their vogue is, I think, entirely due to a want of appreciation of the fact that most cases do uncommonly well without any special treatment. I have had admirable results from restricting local treatment to the application of vaseline or boracic ointment. Perhaps a little more comfort may be given to the patient if ichthyol or magnesium sulphate are used, but they exert no specific action. As regards general treatment, suitable nourishment, and stimulation when necessary, is usually all that is required.

When the tension of the skin is extreme, as sometimes happens when the oedema is very great, free incisions must be made. This is especially necessary if superficial necrotic areas appear as the result of the tension. Too often the incisions themselves slough, but once the pressure is relieved by the local depletion the rest of the skin remains healthy. Abscesses in the eyelids or any other situation should be opened at once. The mouth of the patient must be kept scrupulously clean, and, as in the other acute fevers, it is well to keep it anointed with boroglyceride or boracic vaseline. Should the erysipelas attack the fauces antiseptic gargles and steam inhalations may be employed. Sucking ice sometimes relieves the intense pain. If there is any sign of laryngeal implication the medical attendant must be prepared to perform tracheotomy. For children with erysipelas of the genital organs and adjoining parts Watson Cheyne speaks favourably of the continuous warm bath, which I can well imagine might be of great service in such cases.

PROPHYLAXIS. Erysipelas is so liable to occur frequently in the same person that we have to consider not only how we may prevent the disease infecting others, but also how the individual is to be protected against recurrent attacks. As regards the first point its chief importance is in relation to surgical cases. Should erysipelas appear in a surgical ward, the case must be isolated at once, the bedding must be thoroughly disinfected, and every precaution taken against carrying the infection to recent wounds. Modern asepsis, as applied to instruments, dressings, and the like, has practically abolished the risk of any serious outbreak among surgical patients. It is probable that infected instruments and the hands of the dressers and nurses were the most potent factors in causing the spread of the disease in the days before antiseptics were employed, and it is well to bear that fact in mind. It is possible, also, that desquamated scales of epidermis occasionally disseminated the infection. This suggests that treatment of the inflamed part with ointments is not only grateful

to the patient himself, but by immobilizing the infected scales may be of real value in preventing the disease in others.

There is, as a rule, not much fear of 'medical' erysipelas infecting other patients in a hospital ward, though the custom to-day is, rightly, to isolate it. Should isolation be impossible, especial care must be taken of any patients who have abrasions or breaches in the skin, such as bed-sores, for instance. The doctors and nurses, moreover, must be careful to cover up any scratches on their hands, and take all possible antiseptic precautions. A doctor who is attending a case of erysipelas should avoid operating or attending confinements, the latter most particularly. I have, however, only once in twenty years seen the disease carried by the medical staff of the Edinburgh City Hospital, although the doctors in charge of the erysipelas wards have performed minor operations all over the house. The exception was a case of diphtheria which developed erysipelas round the puncture made by the serum syringe. The medical man who gave the injection had several dressings to do daily in the erysipelas wards at the time. Considering the many thousand injections given during all those years, the risk appears infinitesimal, if ordinary care is taken.

If the patient is isolated he should be detained till all desquamation has ceased. After that is complete, there is probably little fear of infection. For his own sake, however, it is well that he should keep his room as long as there is any œdema or thickening in the parts which have been attacked.

As regards the future of the patient himself, we need only consider those cases in which the disease is said to be *habitual*, that is to say, occurring annually or even more frequently. In this class of patients the dermatitis usually starts at the same point, and this is very often a place which is excoriated by discharges from, for instance, the nose, eye, or ear. Cracks and fissures form in the skin, and harbour the streptococcus, and sometimes the disease gets lighted up by the patient scratching this irritable spot. The most obvious precaution is to remove the cause, that is to say, to get the discharge properly treated, and if possible prevented. Secondly, everything should be done to prevent cracking of the skin. Thus Lenhartz has had good results from recommending the patient to rub the parts nightly with cold cream, and to place a small piece of the cream in each nostril. Many patients would be glad to regularly carry out so simple a prescription, which could be applied equally easily to the ear or to the inner canthus of the eyelid. Thirdly, the patient must be instructed to resist the habit of scratching, which in most cases is doubtless the exciting cause. I have already mentioned how, in a chronic case, placing the arms in splints was followed immediately by improvement, and this principle

may be extended to the prevention of relapses and recurrent attacks, only we must be content with 'moral' rather than literal restraint of the arms. The avoiding of prolonged exposure to extremely cold winds, which may possibly depress the resistance, might also benefit patients subject to erysipelas who have cracks and sores in the neighbourhood of the nostrils.

I have for some years been endeavouring to secure the immunization of this class of patients by the use of *prophylactic vaccines*. If possible these are autogenous. Otherwise a polyvalent stock streptococcal vaccine has been used. The results have so far been encouraging without being brilliant. In one young man, who had 7 attacks and relapses in fifteen months all treated in hospital, an interval of over a year elapsed before his next infection, when he received vaccine again. I have seen nothing of him for six years, but it is possible he may have had more attacks without my knowledge, if he has left the city. Other patients have had no further trouble so far, while at least two have not been favourably influenced. I am inclined to believe that with larger doses good results might be obtained. So far my dosage has run from 20 to 60 million cocci, given at intervals of not less than 5 days for about 6 or 8 weeks. The total number of patients I have so treated is under a dozen, and several have been lost sight of, so one cannot lay stress on the results.

CHAPTER XII

WHOOING-COUGH

Etiology : bacteriology.

Infection and Dissemination.

Pathology.

The Blood in Whooping-cough.

Incubation Period.

The Invasion or Catarrhal Stage.

The Paroxysmal Stage.

Convalescence.

Complications and Sequelæ : hæmorrhages, Prophylaxis : protective inoculation.

ulcer of frænum, digestive troubles,
respiratory complications, nervous com-
plications, sequelæ. Second attacks.

Diagnosis.

Prognosis.

Treatment : management, diet, drugs ; spe-
cific therapy : serum, vaccines ; treat-
ment of complications.

Synonyms—Pertussis, Chincough. *French*, Coqueluche. *German*, Keuch-
husten.

ETIOLOGY. Whooping-cough, usually endemic in our large cities, is apt to occur in widespread epidemics at short intervals of from two to four years. The disease, though no doubt more common, as it is more severe, in northern climates, has been carried practically all over the world. The period of its greatest *seasonal prevalence* has been said to be from January to April. In Edinburgh, so far as I can judge from hospital admissions, it is more common from April to July. No doubt the varying climatic conditions in different cities will cause some difference in the period of its maximum intensity, and it must be regretfully admitted that in Edinburgh we suffer from a 'late' spring. As regards *age*, whooping-cough, of all the infectious diseases, is the most liable to attack infants and very young children. Its age incidence is appreciably lower than that of measles. Thus Brownlee, analysing some 5,000 cases treated in the Glasgow Fever Hospitals, noted that the first year of life furnished even more cases than that succeeding, and that the largest number of patients were in their fourth year, the numbers dropping rapidly from that time onwards. The large proportion of infants of less than six months who suffer from the disease is another feature which distinguishes whooping-cough from measles. Brownlee's table shows no less than five babies of under one month as suffering from the infection, and twenty-nine in all under three months old. After the age of four a marked drop in the numbers affected occurs with each year, and after ten years

patients are extremely few. No period of life, however, is absolutely exempt, and cases have been reported which occurred in persons over the age of eighty. The relative immunity of adults would appear to depend, as is the case in measles, on the protection afforded by an attack in early life, and, doubtless, to a lesser extent on the fact that adults are less likely to be in close contact with affected persons.

Sex certainly appears to exert some influence, females at all ages being somewhat more frequently attacked than males. This is shown in all my own annual returns, and also in the tables of Brownlee. The majority of females is not so marked in the early years of life, but it is still striking. Among adult patients, females greatly predominate, the reason, no doubt, being that women are much more likely to be brought into close contact with affected children than are men. Many of my adult patients have been nurses, nursemaids, or mothers of whooping-cough patients. Doctors also occasionally contract the infection in the course of their duties.

Bacteriology. It may be said that the bacillus described by Bordet and Gengou in 1906 is now generally accepted as the causative micro-organism of whooping-cough. It is found in the sputum, in which it can be detected in 'smear' preparations, but has only exceptionally been recovered from the blood. It occurs in the form of minute oval rods, showing a tendency to stain at the margin and extremities. It is Gram-negative and, resembling in some ways the influenza bacillus, is less pleomorphic than that organism. It may be stained with carbol-fuchsin or carbol-methylene blue.

The claim of this bacillus to specificity rests on the facts that it is agglutinated by the serum of convalescents and that it also gives the complement-deviation reaction with such a serum. Klimenko, moreover, has succeeded, by means of intra-tracheal injections of pure cultures, in infecting puppies and monkeys with an illness which, accompanied by pyrexia, respiratory catarrh, and broncho-pneumonia, follows after a period of incubation. These inoculated animals gave the same disease to healthy young dogs. The general belief that the Bordet-Gengou bacillus is really the cause of the disease is evidenced by the extensive use of the micro-organism in vaccines used for therapeutic and prophylactic purposes. The fact that it is more readily found in the catarrhal than in the paroxysmal stage is quite in accordance with clinical experience regarding the infectivity of whooping-cough.

Infection and Dissemination. Whooping-cough is highly infectious and is usually transmitted by actual or virtual contact from person to person. The virus is contained in the expectoration, and no doubt also in

'droplets' from the mouth, of an infected person and is, it may be supposed, inhaled directly by the recipient. We know little about the infection, but facts point to it being short lived outside the human body. None the less it can be carried on fomites, particularly on the clothes of attendants, and thus communicate the disease through the medium of a third person. As is the case with measles, it is the invasion, or catarrhal, stage which is most infectious, and this unfortunately is the period at which the nature of the illness can, as a rule, only be guessed. The infectivity is, no doubt, hardly so great as that of measles, but, when we consider that most children suffer from the illness, and that often at their first exposure, we must assume that it is extremely high. When the paroxysmal stage is reached, however, there is, so far as my experience goes, but little risk of the patient infecting others. I have frequently had patients in this stage in both our scarlatina and measles wards, and have never seen any harm result, even when large numbers of susceptible children were exposed. This is perhaps partly due to the children being kept in bed, and to the chances of direct contact being thus considerably reduced, but whenever a patient is admitted in the unrecognized catarrhal stage, and is treated under exactly similar conditions, trouble invariably follows. Particularly is this the case in measles wards, where it is natural to expect that the respiratory tract of the patients is peculiarly vulnerable. I am inclined, then, to believe that when the whoop has once properly developed, the risks of infection are very slight, and can be rendered even less by careful attention to the disposal of the sputum. This view is supported by experience at the Edinburgh Children's Hospital, by the observations of Weill, Guérassimovitch, and others, and also by the recognized difficulty of recovering the bacillus after the whoop has developed.

PATHOLOGY. The causative micro-organism probably affects the respiratory tract and obtains a nidus in that situation. The disease, however, is much more than a mere laryngeal or bronchial inflammation. We cannot watch a case of sharp whooping-cough without being convinced that the patient, in addition to his local manifestations, suffers from some degree of toxæmia, and that his nervous system is profoundly affected. This nervous irritability has caused some authorities to regard whooping-cough more as a neurosis than as a specific disease, and quite recently Czerny, and also Döbeli, have maintained that the catarrh, which may be due to a variety of micro-organisms, may be transmissible from person to person, but that the type of the paroxysms are the result of a 'psychical infection'. Döbeli, indeed, goes so far as to say that the infected child must have heard, and probably seen, the typical paroxysms of another, a suggestion which must be contradicted by the experience of almost any one who has had charge of wards in

a children's or fever hospital. It is not unusual for a child to be isolated, on the evidence of a blood count, before the paroxysmal stage has commenced, and yet other children, even infants of under six months, will take the disease and whoop typically before they have had the opportunity of, so to speak, studying in others what they are expected to do. That suggestion, imitation, and habit play some part in determining the onset, number, and duration of the paroxysms of children who already undoubtedly suffer from the disease may be freely admitted, but I think we may safely discard the 'psychical infection' theory.

Mallory, who has been able to demonstrate that the cilia of the lining cells of the trachea are matted together and, as it were, clogged by masses of the Bordet bacillus, holds that the mucus secretion, instead of moving upwards, gradually collects until it has to be expelled by a paroxysm of coughing. Previously other observers had noted the appearance of a tough pellet of mucus lying in the neighbourhood of the glottis before the paroxysm which they attributed to the efforts to expel it. Bordet states that the toxin of his bacillus is capable of causing necrotic changes in the respiratory passages and that the persistence of the cough is due to lesions in the lining of the bronchi. No doubt the vagus and recurrent laryngeal nerves are particularly irritated by the action of the toxin, and it would seem that this alone might account for the paroxysms and the subsequent vomiting. Zangger attributes them to the action of the toxins in the spinal cord and reflex action transmitted through the vagus to the lungs and larynx.

Morbid Anatomy. Unless complications have supervened there is nothing typical to be found on the post-mortem table. Cerebral congestion and actual hæmorrhage have been noted in some instances. Enlargement of the bronchial glands may be seen, and patches of broncho-pneumonia or atelectasis with some emphysema are common in fatal cases.

The blood in whooping-cough. The blood presents somewhat well-marked characteristics which may possibly be utilized to aid diagnosis. A high leucocyte count is a feature of the illness from the onset. Crombie found that the average count during the preliminary catarrhal stage was over 20,000 in the twenty-four patients examined. The lowest count was 7,600, the highest, 85,000. In the paroxysmal stage the average exceeded 22,000 leucocytes. This leucocytosis is maintained till the whoops become less frequent and the severity of the disease diminishes. In mild cases, however, the count may be only slightly above normal. The lymphocytes are always increased either absolutely or relatively, and this is the distinctive point to be gained from the examination of the blood. During the acute stages of the illness the percentage of polymorphs and lymphocytes may be said to

be inverted, and the increase in the latter appears to correspond with the severity of the attack. In the cases examined by Crombie in the catarrhal stage the maximum polymorph percentage was only 50. The average lymphocyte percentage was as high as 66 and the maximum was 84, and these figures were exceeded in the second week of the paroxysmal stage, for which the percentages were 67 and 88 respectively. When broncho-pneumonic complications are present the leucocytosis may be so extreme as to suggest leucæmia. Cabot reports a case where the white count was 185,000, and Crombie one of 141,000. In one case, fatal from convulsions, 223,000 leucocytes were noted. On the other hand, in one case of broncho-pneumonia there was leucopenia. The value of these observations is that in hospital they may be utilized when a patient is suspected to be in the catarrhal stage.

INCUBATION PERIOD. This stage of whooping-cough seems very variable, and it is difficult to define its limits owing to the want of exact data. I have no observations of my own on which I can rely with any confidence. The insidious commencement of the catarrhal stage often leaves some uncertainty as to the actual day on which the first symptom occurs. There seems no doubt, however, that the period is not infrequently as long as thirteen or fourteen days, and Fagge reports a case of this kind. On the other hand, Gerhardt and others maintain that the incubation stage may be as short as one or two days, and many writers state that most cases have a latent period of between five and eight days. All we can assume, then, is that this stage varies from a few days to a fortnight, and, for practical purposes, that a person, who fifteen days after the last exposure presents no symptoms of catarrh, is free from the risk of developing the disease.

THE INVASION OR CATARRHAL STAGE. The first symptoms are those of an ordinary catarrh, coughing being the most prominent feature. In some cases there is sneezing, coryza, and lacrymation. A slight degree of fever is not unusual, and its type is most often remittent, with evening rises. As regards other manifestations much depends on the severity of the attack and the character of the epidemic. The children, as a rule, take their food fairly well, but in sharp cases the appetite may be lost. There is probably a greater or less degree of malaise, and many patients are dull and lose interest in toys and games. Others complain of headache, and the sleep is usually broken and disturbed. The cough is of a short dry variety, and occurs almost at any time, not showing, at this early period, the subsequent tendency to space itself out into paroxysms at more or less regular intervals. The persistent character of the cough, its gradually increasing severity, and its great frequency per minute, when it has once started, sometimes suggest that the patient is suffering from something more than a mere

bronchial catarrh. Laryngitis is occasionally noticed during this stage, and hardly a year passes without a whooping-cough patient in the catarrhal stage being sent into the Edinburgh City Hospital in mistake for diphtheritic croup. Towards the end of the invasion period the patient often begins to vomit after a fit of severe coughing, his attacks occur at more regular intervals and assume a more paroxysmal type, and this accentuation of his symptoms is usually most marked at night. The catarrhal stage is in severe cases much curtailed, and lasts only a few days. On the other hand, it has been reported, in rare instances, as continuing for as long as six weeks. From about eight to fourteen days would appear to cover its usual limits.

THE PAROXYSMAL STAGE. The most prominent feature of this stage is the occurrence of paroxysms at more or less frequent intervals. These paroxysms may vary much in number and in severity. They may occur only once or twice in the twenty-four hours, or in very severe cases may appear every half-hour. Very rarely, however, are there more than twenty-four paroxysms a day, and in an average case the number is from ten to fifteen during the height of the illness. The **paroxysm** consists of a large number of short expiratory coughs, as if the patient was trying to expel something lodged in his larynx. The coughs come in very quick succession, giving the patient no time to make any inspiratory effort between them, and are repeated like the firing of a machine-gun or the explosions of a motor-bicycle. After a varying number of these short coughs an interval occurs during which the patient attempts, with more or less success, to draw breath, and sometimes at once, sometimes after a minute's struggle or even longer, the air is inspired through the apparently tense vocal cords, causing a somewhat prolonged crowing sound which constitutes the typical *whoop*. In an ordinary paroxysm the whole process is repeated several times, the explosive coughs being followed by the inspiratory crow on each occasion. In mild cases there may not be more than one whoop. In severe ones, on the other hand, a dozen or more are not uncommon. With the successive spasms of coughing the distress of the patient becomes more acute. The face, at first flushed, becomes congested, purple, and swollen. Tears stream from the injected and starting eyes. Strings of tenacious mucus hang from the nostrils, and a large amount of glairy material, sometimes tinged or streaked with blood, is expelled from the mouth. The tongue, swollen and purple, protrudes in the effort of the cough, and occasionally the sphincters are relaxed, with involuntary passage of urine and fæces. At last comes a vomit which, by emptying at once both the stomach and tubes, usually gives immediate relief. Vomiting, however, is not an invariable symptom, and, curiously enough, as Eustace Smith has pointed out, it

occasionally precedes instead of following the spasm. The process is a very pitiable one to witness. The patients are usually so small and obviously suffer so much, and their anxiety and fear is so well marked, that they cannot fail to enlist the sympathy of the onlooker. After the paroxysm is over, the child, who has during it assumed the sitting position, sinks back exhausted, usually perspiring profusely and often sobbing. As a rule a period of complete rest follows, and many children fall asleep almost at once.

In severe cases, in which, during the paroxysm, the whoop is delayed for perhaps more than a minute, the appearance of the patient may be most alarming. He is unable to take the necessary inspiration, though all his extraordinary muscles of respiration may be visibly working to that end, and he appears, as it were, choking. Occasionally, indeed, actual syncope occurs and, in very rare instances, even death. As a rule relaxation of the glottis occurs in time to prevent a fatal result. Such a paroxysm in some cases terminates in an actual convulsion, and in others a convulsive seizure seems to take the place of the paroxysm itself.

✓ A curious feature is the obvious premonition experienced by many patients. Sometimes this would appear to be an actual aura. In most cases it is more likely that a sensation of tickling in the chest or the larynx warns the sufferer that a paroxysm is impending, and he does his best to postpone as long as possible the inevitable cough. In some patients a sensation of constriction of the chest is the first warning. Others may yawn or sneeze, and some become dizzy. Occasionally the first premonition may occur a quarter of an hour before the spasm; usually it only precedes it by a few minutes. The child often commences to cry, and this precipitates the paroxysm at once. Many patients will try to breathe cautiously, and no longer take full respirations for fear of exciting the cough. When it becomes inevitable they usually attempt to hold on to somebody or something. The giving of food, any time shortly before a paroxysm may be reasonably expected, will usually cause it to appear. In a hospital ward, when one child starts to whoop it is common to see many others follow its example, probably from suggestion.

On the other hand, fright or different mental emotions are sometimes capable of inhibiting the spasms. The wife of a German general is stated by Sticker to have claimed that she could cure whooping-cough by the judicious use of the rod, a method of treatment which is not likely to commend itself to physicians, but which in prolonged cases where the whooping is maintained as a habit would conceivably be effective. I have often noticed that the presence of a large clinic in the wards will stop many patients from whooping, even when a paroxysm is due, and when they are encouraged

by being given something to drink. The departure of such a class of students from the wards is often the signal for a general explosion of whoops all round. Mental conditions, then, undoubtedly have some influence on the occurrence of the access of coughing.

Throughout this stage the paroxysms are most severe and often most numerous at night. The child wakes suddenly from sleep and assumes a sitting attitude, and the cough follows at once. Usually sleep is obtained between the spasms.

As regards the general condition of the patient, much will depend upon the number and severity of the paroxysms and on the age and strength of the patient. The average child of more than two years old is, if no complications are present, reasonably well between his attacks. The pulse, often much accelerated during the spasm, regains the normal, and the patient will play contentedly with his toys, enjoy his meals, and present quite his ordinary appearance. If, however, the paroxysms occur extremely frequently and are of a prolonged nature, he remains apathetic and dull in the intervals, and the constant strain of coughing sets its distinctive mark upon the face, which becomes pale, swollen, and puffy, with œdematous eyelids and somewhat dusky lips. The facies is, indeed, often quite characteristic, and the expression is weary and woebegone. When there is much vomiting and the whoops are frequent, marked wasting is evident, and some infants die of marasmus. Rickety and badly nourished children bear the strain of whooping-cough badly.

There is seldom any fever at this stage of the illness except in the presence of complications. There is much nervous irritability, and sometimes even a touch or the turning of the patient in bed will excite the whoop. Some children refuse food altogether, dreading the inevitable paroxysm which may follow any attempt to give it.

The paroxysmal stage lasts for a varying time, but a fair average would be about six weeks. It is probably at its worst in the second and third weeks, and thereafter the spasms are in many cases less frequently repeated and are, in themselves, shorter and less severe.

CONVALESCENT STAGE. The whoop often persists for a long time, even after the patient is quite well. It may only occur once or twice in the twenty-four hours, and that usually at night. How far this is not a matter of habit is open to question. Some children will whoop typically, though probably without vomiting, for nearly a year after their attack. Especially is this the case if any ordinary catarrh or an attack of measles supervenes within a few months of whooping-cough.

COMPLICATIONS AND SEQUELÆ. Under this heading we may

first consider the *hæmorrhages* which occur with such comparative frequency in the course of whooping-cough as to be rather regarded as symptoms of the disease. The great strain of coughing often causes œdema of the eyelids, as we have already seen, and less frequently hæmorrhages in different situations occur from the same cause. Epistaxis is common enough, and much of the blood which appears with the expectoration doubtless comes from the nose, but the streaks seen in the sputum are, in my opinion, occasionally due to the rupture of minute blood-vessels in the congested respiratory tract. Blood from the nose, also, is no doubt often swallowed, and it need not be assumed that hæmorrhagic vomited matter is the result of gastric bleeding. Hæmorrhage into the conjunctiva occurs in perhaps 2 per cent. of the cases. It is ugly to look at, the whole white of the eye being often masked with a thin layer of bright red blood, the cornea alone being unaffected. Smaller bleedings, involving only small areas of the conjunctiva, are more frequently seen. Such hæmorrhage is very disfiguring to the patient and may take four or five weeks to absorb. I have never seen the 'tears of blood' described by Trousseau as occurring in bad paroxysms. In such cases, no doubt, the hæmorrhage comes from the conjunctival vessels. Bleeding into the eyelids and a resulting 'black eye' occasionally occur. The first time I saw this complication it was difficult for the nurses to convince me that the patient had not received an injury, but I have seen many instances since. Much more rarely does bleeding occur from the ear, the blood trickling slowly out during the paroxysm. I have only met with two patients, out of considerably more than two thousand, in which this occurred. In their case, as in some others reported, the tympanum was not ruptured, though this has been noted by some observers. Hæmorrhage into the skin, with true purpuric spots, is very uncommon, and is only likely to occur in very weakly patients with a predisposition to bleed. Both meningeal and cerebral hæmorrhages have been reported.

The strain of the coughing is also responsible for the *prolapse of the rectum* which is not uncommonly observed, occurring in nearly one per cent. of hospital cases. Another not uncommon result is *hernia*, of which I have seen many examples both inguinal and umbilical. Cardiac dilatation and emphysema are due to the same cause.

Just as hæmorrhage occurs mechanically as the result of great vascular congestion, so another very frequent concomitant of whooping-cough, *ulcer of the frænum*, is the result of mechanical injury to the under surface of the tongue. It is seen particularly in young children who have cut their two first lower incisors, and in whom during the effort of coughing the

protruded tongue is pressed against the edges of these teeth. First merely a transverse tear, or an abrasion, it develops into a greyish oval patch of ulceration on the under surface of the frænum. It lasts during the paroxysmal stage, never appearing before the whoops are well developed, and heals readily and quickly in convalescence.

Digestive troubles are common. The frequent vomiting seen in the disease is merely the effect of the paroxysm, but occasionally it may occur independently of, and between, the spasms. Sometimes, again, in cases where the interval between the accesses of coughing is two hours or more, the food may be rejected quite undigested, and there is every reason to believe that in many instances gastric digestion is extremely weak. The stomach often contains large quantities of thick ropy mucus, and this, together with imperfectly digested food, is apt to cause a looseness of the bowels, and in some instances severe diarrhœa. A certain amount of digestive trouble may be of little significance in an otherwise healthy child, but it much increases the difficulty of adequately nourishing children who are naturally weakly or who have been exhausted by a prolonged and severe paroxysmal stage.

The urine is usually pale and of a low specific gravity. Albuminuria, so far as my experience goes, is uncommon, and nephritis extremely rare. According to some observers, however, both albumin and sugar are frequently present in the urine.

Respiratory complications are the chief cause of death in whooping-cough. We must regard some degree of *bronchitis* as a natural occurrence in the catarrhal stage, and so long as the condition is limited to the larger tubes it is of no importance. It often persists during the paroxysmal period, and unless the small tubes are involved is not likely to affect the temperature. Between the accesses there is often little to be heard at this time except a few coarse sounds. *Laryngitis*, again, is not uncommon in the catarrhal stage and need hardly be regarded as a complication. Occasionally it is severe enough to seriously embarrass the breathing. *Broncho-pneumonia*, as is the case in measles, is the most important and most fatal of the complications. As has been said in discussing the latter disease, it is impossible to say with accuracy at what point capillary bronchitis ends and pneumonia begins. The lung tissue is almost certainly involved in all these cases, and when atelectasis occurs it is usually associated with a broncho-pneumonic condition (see chapter on Measles, p. 46). The general course of the inflammation is similar to that of measles, and the reader is referred to the chart on page 48. With the onset of broncho-pneumonia the respirations rise rapidly, and in young children may be

sometimes as high as 80 or even 100 to the minute. The pulse is also increased, but not as a rule in proportion to the acceleration of the respirations. Rates of 150 to 170 are, however, common. The temperature is very variable, but often attains high levels at night. The face is often pale, and presents a slight or well-marked cyanotic tinge, and the *alæ nasi* expand on inspiration. Areas of dullness may or may not be detected in the chest, and fine crepitations are found scattered over the lungs in different situations. Sometimes the coalescence of various affected areas will cause a considerable patch of dullness, even large enough to suggest the presence of a lobar pneumonia. With the lung inflammation the typical whoops cease, or are very much reduced in frequency, but a troublesome cough continues, with copious expectoration of tenacious and sometimes blood-stained material. Vomiting and diarrhœa are only too commonly seen.

Areas of dullness in infants are often due to *atelectasis*, and this sudden collapse of the lung tissue after a severe paroxysm, owing to blocking of one of the tubes with tough mucus, may be responsible for sudden syncope, death, or convulsions. The child falls back pale and cyanosed, and the respiration becomes shallow and rapid. The skin is cold and often clammy with sweat. With improvement in these acute pulmonary conditions the paroxysms return, and the case runs its ordinary course. In very young children, however, broncho-pneumonia is almost invariably fatal.

The most characteristic time for the pulmonary inflammation to occur is in the second or third week of the paroxysmal stage. According to some observers, however, the time of greatest risk is when the paroxysms are growing less frequent and severe, and the patient entering upon convalescence. This no doubt might be explained by the care taken of the patient being likely to be relaxed at this period.

Lobar pneumonia is a rare complication. In a series of 1,069 consecutive cases it only occurred three times. All the patients made a good recovery, the disease being trivial when compared to broncho-pneumonia. *Pleurisy* with effusion occurred in a similar number of cases, and is met with chiefly in older children, above five years of age, and adults.

Some degree of compensatory *emphysema* may be regarded as usual in cases of broncho-pneumonia and collapse. It is to be found at the upper part of the lung, the other conditions chiefly affecting the base. In very severe cases rupture of the lung and pneumothorax, and even subcutaneous emphysema, have been reported. In the latter case, of which I have seen three examples, it is under the skin of the neck and face that the crackling sensation is likely to be found, the air finding its way from the root of the lung into the mediastinum. Bronchiectasis has also been described.

Nervous complications. *Convulsions* very frequently are observed in whooping-cough, and, next to broncho-pneumonia, they are the most common cause of a fatal termination. The French authors distinguish what they term *convulsions internes* from *convulsions externes*, meaning by the former those instances of spasm of the glottis which are accompanied by convulsive movements and followed by asphyxia and unconsciousness. These, as a rule, may be regarded as examples of an extremely severe paroxysm and its effects upon a poisoned nervous system. Fits, however, are often seen even in comparatively mild cases of whooping-cough, and may appear quite independently of the spasms. They are most frequently observed in teething infants, and doubtless any small irritation is often sufficient to produce them in children who suffer from the nervous excitability so characteristic of the disease. At other times they appear to mark the onset of some complication, and they are not infrequently associated with the collapse of an area of lung tissue. They have been also attributed to cerebral hæmorrhage, meningeal hæmorrhage, and thrombosis of the brain sinuses. In many instances, I think, they may be regarded as due to the toxins of the disease, and in those cases which I have been able to examine after death I have never come across any gross lesion. Cerebral hæmorrhage has also been said to occur as the result, and not the cause, of a fit.

The convulsions vary much in severity. Some are distinctly localized, one limb suffering most. In others the whole body participates in the seizure. The eyes usually become fixed and are often turned inwards. The pupils are dilated and the face pale. The spasms themselves may be clonic or tonic in character. Rigidity of the extremities with the thumbs turned into the palms is frequently noticed. In some cases the fit is prolonged for a quarter of an hour or more and then the muscles relax, the child regaining consciousness or relapsing into a state of coma. Convulsions may occur singly, or may be repeated at short intervals till death. In my experience they appear most often in patients with a broncho-pneumonic complication, but they are not rarely observed in uncomplicated cases, especially in rickety patients.

Severe forms of nervous disease have been described as following, or complicating, an attack of whooping-cough. Different varieties of neuritis, hemiplegia, and ascending paralysis may be mentioned as examples. They are, however, fortunately rare, and have not occurred in my own experience. Blindness, loss of memory, and mental disturbances sometimes follow the disease, but these have been attributed by some authors to a misuse of drugs, particularly narcotics and belladonna. Ophthalmoplegia and optic neuritis have also been reported.

Sequelæ. During the paroxysmal stage there is sometimes some degree of *cardiac dilatation*. In most instances this leaves behind it no permanent damage, but Osler mentions cases of lasting injury and even of severe valvular disease resulting from the heart strain which accompanies the illness. Of other conditions *enlargement of the bronchial glands* may be mentioned. This has been stated by some writers to be constant in whooping-cough, and one of the theories advanced to explain the causation of the paroxysms is the pressure of these glands on the vagus. Persistence of this enlargement is possibly responsible for some of the later sequelæ such as chronic bronchitis, asthma, and tubercle. *Otorrhœa* is not infrequently seen in debilitated children towards the end of an attack, and the cervical glands may be enlarged. The most important sequel of the disease is *tuberculosis*, which frequently supervenes in a prolonged broncho-pneumonia, and usually runs a comparatively rapid course. Rickets is also said to follow whooping-cough in some cases. The patient's chest may remain permanently deformed after a bad attack, and chronic bronchitis with emphysema and asthma, as noted above, may persist as legacies of the illness. Children may continue to be nervous for a long period. They are often easily frightened and afraid of the dark, and any slight catarrh from which they may suffer is liable to be mistaken for a recrudescence of whooping-cough itself.

Second attacks of whooping-cough are extremely rare. I have never met with one myself, and, judging from the comparative frequency with which cases are admitted to hospital with an incorrect diagnosis of the disease, little weight can be attached to the history given by parents that a child has had a previous attack, unless, indeed, facts confirming it can be obtained from a competent medical man. The protection afforded by the disease is, indeed, probably greater than that observed in connexion with other acute infections.

DIAGNOSIS. In the catarrhal stage this is often difficult, if not impossible. The presence of an epidemic or the history of exposure should be sufficient to arouse suspicion if a patient is suffering from a febrile catarrh with frequent irritating cough. Towards the end of this stage the tendency for the cough to be less constant, but more paroxysmal, with comparatively long intervals of relief, and the well-marked exacerbation of the accesses during the night, will make the diagnosis fairly clear, and the occurrence of vomiting after the spasm is always a suspicious feature. The first actual whoop nearly always occurs during the night. The gradual exacerbation of the cough, in spite of treatment, should distinguish this stage from ordinary catarrh. Although it is obvious that blood examinations are

hardly possible for the busy general practitioner, it is unquestionable that at this early period of the disease they have a very real value for those in charge of wards in children's or fever hospitals. The well-marked leucocytosis and the very marked increase in the percentage of lymphocytes are, in a doubtful case, highly suggestive, and I consider it advisable to at least examine a film of the blood of any suspicious patient. My experience has been that the disease in the invasion stage is extremely infectious, and even a troublesome method of diagnosis is better than none at all.

In the paroxysmal stage the diagnosis is, as a rule, easy enough. Any one who has once witnessed a typical access will readily recognize it again. But it must be remembered that the disease may be present, and yet truly typical paroxysms may not occur. Thus, such a symptom as the final vomit is not infrequently absent, or, again, the whoop itself may be missing, the inspiration being made without the characteristic crow. In such cases we must judge by the general explosive nature of the paroxysm, and particularly by the suddenness and unexpectedness of its onset. This is not a case of an irritating cough gradually increasing till the patient gasps or vomits and struggles in his efforts to expel some substance sticking in his throat. From the moment of onset of the true paroxysm the patient rattles out his coughs with great rapidity and with no time for inspiration. Should these attacks be more frequent and worst at night, our suspicion of whooping-cough will be probably confirmed. The examination of the chest may also help us. 'In a doubtful case', says Eustace Smith, 'the marked contrast between the insignificance of the physical signs and the frequency and violence of the cough is by no means without its value in diagnosis.'

When the medical attendant is not present during a paroxysm it is always worth while, particularly in young children, to examine the under surface of the tongue and search for the ulcer of the frænum, which, if present, will confirm to some extent the diagnosis. It is not, however, absolutely pathognomonic of whooping-cough, being occasionally, if rarely, caused by accesses of coughing dependent on some other cause, and, of course, it is by no means always present. The appearance of the patient, again, will often attract attention, but, it must be confessed, we are not likely to see much puffiness of the face or cedema of the eyelids in really doubtful cases. An attempt should be made to examine the throat, not so much because there is likely to be anything to be seen, but because it gives us a decent opportunity of deliberately attempting to excite a paroxysm. Moreover, whooping-cough is sometimes simulated by the cough caused by enlarged tonsils or naso-pharyngeal catarrh.

As regards **differential diagnosis**, in the catarrhal stage the disease may be mistaken for measles, especially if any coryza is present. The non-appearance of a rash in five or six days and the absence of Koplik's spots make a sufficient distinction. Foreign bodies in the larynx have caused accesses of coughing which have been mistaken for whooping-cough. Tubercular disease of the *bronchial glands* is, according to Comby, the illness most likely to cause confusion. To recognize whooping-cough we must lay stress on the presence of an epidemic, and the freedom of the patient from tubercular glands in the neck and axilla. Physical signs, moreover, are usually absent in the intervals, and there is little or no fever in the ordinary whooping-cough case. During the recent epidemics of *influenza* I have frequently had great difficulty in distinguishing the paroxysms of coughing in children with that disease from whooping-cough; the actual whoop, however, is not present. Laryngismus stridulus is hardly likely to be taken for whooping-cough, but it appears that the mistake has been made. Sticker emphasizes the necessity of being on the look out for hysterical imitations of the disease. In these, both the expectoration and the vomiting are conspicuously absent, and the access may last much longer, even for an hour. Such results as ulcer of the frænum or puffiness of the eyelids are never seen. The preliminary catarrhal stage is, moreover, absent in these imitative cases. We must also remember that second attacks of whooping-cough are extremely rare, and that, therefore, a condition closely simulating it, in a person who has previously suffered from the disease, is almost certainly not a true case. We have already noted that some children acquire a habit of coughing during an attack which may afterwards remain evident in any ordinary catarrh. In hospital practice an examination of the blood may assist the diagnosis.

PROGNOSIS. Those who only see whooping-cough in good-class practice do not, perhaps, realize how serious it is liable to be in the children of the poor. Everywhere the disease is a dangerous one, though it is not improbable that we see it at its worst in Scotland. For the decennial period ending 1910, for instance, the death-rate per thousand persons living was 0·27 for England and Wales, 0·44 for Scotland, and 0·42 for Edinburgh. The compulsory notification recently introduced in England will give us accurate figures of the case death-rate, which has been computed as being under 5 per cent. When we remember that, widespread as the disease is, the children of the better classes usually recover, it is obvious that the lower classes suffer very severely indeed. The hospital death-rate is always a high one. No doubt only the worst cases reach hospital and the majority have developed some complication before admission. For a period of eight years,

ending in 1900, the City Hospital death-rate was 18·11 per cent., and that this is not an extraordinary figure is proved by the fact that, over a period of twenty-two years ending in 1899, there was a death-rate of 18·3 per cent. in the Glasgow Fever Hospitals among the 5,000 patients treated. D'Espine, moreover, has collected statistics showing the mortality in children's hospitals, and states that it is 11·1 in his own clinic at Geneva, 20·7 at Lausanne; in Paris 18·1 at the *Enfant Malades*, 23·1 at the Trousseau, 23 at the Bretonneau; in Berlin 23·6 in Baginsky's clinic at the Kaiserin Friedrich and 27·9 per cent. at the babies' hospital at Weissensee. For a period of ten years, ending in 1914, our own statistics have been considerably better, the total case-mortality in a series of 1,841 patients being 13 per cent., a distinct improvement having followed the removal of the hospital to the country.

The prognosis is much influenced by the *age* of the patient. The Glasgow mortality is given by Johnston as 35 per cent. for the first two years of life, 22 per cent. for the third year, 12 for the fourth, 8 for the fifth, and 6 between the ages of five and ten years. Over ten years the mortality is very trifling, though it is obvious that the illness must be regarded seriously in aged persons. My own experience tallies with that of Johnston, though my figures suggest that the first year of life is more fatal than the second, and that the third is only slightly less dangerous. It may be added that the mortality of very young infants is slightly less than those of over six months. Although the hospital mortality is no guide to the general case death-rate from the illness, it emphasizes the fact that the risks become less as age advances.

It is usually stated that, just as the disease attacks a higher percentage of females than of males, so the former *sex* furnishes an undue proportion of the deaths. But Johnston's table shows only a difference of five decimal points in favour of the males, and in my own series of 1,841 patients the case-mortality of females was 12·2 as against 13·9 per cent. for the males.

The prognosis will also vary with the general condition of the patient at the time of his attack. Rickety children seldom do well, and those with any predisposition to chest trouble are very liable to take bronchopneumonia. Nervous patients, again, especially children who have suffered from fits at the time of dentition, will be more likely to develop convulsions. A weakly, badly nourished child, if under three years of age, is hardly likely to survive a severe attack.

It is generally admitted that, the longer the catarrhal period, the milder the paroxysmal stage is likely to be. In really bad attacks the onset of the whoop is not long delayed. During the height of the illness the gravity of the condition may be roughly estimated by the number and severity

of the spasms. The more frequent and prolonged these are, the greater the risk to the patient. But even if they are extremely numerous and very severe, always provided that the patient seems perfectly well between the paroxysms, we need not feel too much concern about his chances of ultimate recovery. A sudden and unexpected diminution in the number and severity of the coughs is not always a good sign, and, if it occurs as early as the third week, should always arouse suspicion that a complication is developing.

It is, in the vast majority of cases, the complications which kill. Occasionally a child may succumb to a spasm of the glottis in the midst of a paroxysm, but such an occurrence is fortunately most rare. Provided, then, no complication supervenes, the outlook is always hopeful. Bronchopneumonia is responsible for most of the deaths. Even in the most favourable circumstances this complication will kill more than a quarter of those attacked by it, and for a long time the mortality of the City Hospital was over 70 per cent. Latterly it has very rarely exceeded 40 per cent. It is unusual for the pulmonary inflammation to last less than three weeks. Bad signs are pallor with purple lips and extremely rapid respirations, say over 70 per minute. The temperature is a poor guide. In many severe cases it may run a quite subacute course. A return of the definite spasms of whooping often announces a general improvement. On the other hand, restlessness and refusal to take food are symptoms of evil omen.

Convulsions, except when they occur at the onset of a pneumonic complication and are not repeated, almost invariably cause death sooner or later. Out of ninety-four cases in which convulsions occurred in the City Hospital, sixty-eight terminated fatally, the mortality being about 72 per cent.

As regards sequelæ an extremely cautious prognosis should be given regarding children who may have a tubercular taint. Whooping-cough is very liable to light up a latent tubercular condition. Patients who suffer from adenoids are likely to be troubled by a return of the paroxysms for a long time, and the same applies to those with an elongated uvula. As regards the paralytic sequels of whooping-cough, should they occur, it has been said that in 40 per cent. of the cases the damage is permanent.

TREATMENT. The general *management* of whooping-cough is a matter of some importance. During the catarrhal stage, if it is recognized, it is well to keep the patients in bed. Later, if the paroxysmal period is unaccompanied by pyrexia, and is not unduly severe, there is no reason why they should not be allowed to get up. Overclothing should be avoided. A warm flannel gown, with perhaps the addition of a flannel binder, should be

sufficient for children who are kept in bed, and for those allowed up it is enough to see that the clothing is both light and warm. To overburden a child with several layers of thick garments encourages sweating, and, as a result, the chill which it is desired to avoid is all the more likely to appear. Various views are expressed on the question as to whether the patient should be permitted to go out into the open air. Many are in favour of granting this liberty if the weather conditions are favourable, and sudden changes of temperature not too marked. Others, again, hold by the principle that a steadily maintained even temperature is most suitable for whooping-cough, and Sticker considers this should not be below 65° F. Many favour the system of nursing a patient in two rooms, one for day and one for night, all ventilation being carried out in the child's absence. The atmosphere of these rooms is kept medicated by vaporizing creasote or eucalyptus in a metal bowl over a spirit lamp.

My own view is entirely in favour of free ventilation. I had a long experience of the other method and, so far as medicated atmospheres are concerned, my results have been infinitely better since I discarded them. I try, so far as possible, to treat my patients under open-air conditions. When it is not raining the patients, in most months of the year, spend their day out of doors. Even in winter all windows are kept widely open, and, short of allowing an actual draught to play directly upon a patient, no attempt is made to exclude currents of air. Whatever may be the case in private practice, there is little doubt of the advisability of this method in hospital wards. Whereas, formerly, broncho-pneumonia often appeared to spread from patient to patient, it is now extremely rare to see a child who is admitted free of that dangerous complication contract it in the wards. Other advantages of open-air treatment will be mentioned in discussing the management of broncho-pneumonia.

For children whose history leads us to the supposition that they are naturally predisposed to chest complications, a light jacket of Gamgee tissue may be prescribed, and the chest rubbed night and morning with some stimulating oil. It is often wiser to keep such patients in bed, but they can be carried in their cots on to the hospital balconies, or into the garden, like the rest. All children should be sponged or bathed frequently, and it is hardly necessary to add that, during this process, the windows should be shut and all draughts carefully avoided. The nurse should remember that, during each paroxysm, she should remain with the child and support it. It adds greatly to the misery of the patient if he is left to suffer unattended. A spittoon or receptacle, containing some harmless antiseptic, should be ready to receive the mucus and vomited matter.

Throughout the disease attention should be directed to the condition of the bowels. Constipation should be corrected without delay. The paroxysms are always likely to become worse in the presence of any irritation in the alimentary tract.

Diet. As the appearance of the whoop is usually the first certain sign of the disease, the question of the diet in the catarrhal stage needs little or no discussion. It is only seldom that patients come under our observation at this early period. If there is any fever a fluid diet is indicated, and this should be of as bland and unstimulating a character as possible. Milk, supplemented occasionally by meat broths, will meet all requirements. In the paroxysmal stage, however, we have to seriously consider the best means of feeding the patient. There are often two difficulties to contend with. Firstly, a paroxysm, coming on shortly after food has been given, is very liable to empty the stomach by the associated vomiting. Secondly, some children learn by bitter experience that the taking of food excites the cough, and, as a result, firmly resist any attempt made to feed them. To force food upon such patients often ends in their acquiring an unpleasant habit of deliberately rejecting from the stomach whatever is given them.

It is not only, however, the risk of the food being vomited, or refused, which has to be considered. We must also recollect that gastric irritation, whether from overloading the stomach or from unsuitable food, undoubtedly excites the cough, and, therefore, whatever is allowed must be given only in small quantities, and must also be very digestible. The stage of the paroxysm, moreover, is often so prolonged and so apt to exhaust the patient that it is highly desirable to supply a liberal amount of nourishment, in order, so far as possible, to prevent the wasting which is often a striking feature of the illness. In hospital practice, particularly, liberal feeding may be of paramount importance from the very first, as the majority of patients have suffered from much vomiting and from improper dieting before admission. The difficulty of giving them sufficient food is in no way lessened by the fact that their digestion has often been temporarily ruined before they came under observation.

There is, of course, a clear distinction to be drawn between children of different ages. Children of over five years of age are, as a rule, not difficult to feed. They are able to run about, and often enjoy a healthy appetite. Unless they are debilitated by a complication, or by previous illness, they are perfectly capable of assimilating an ordinary light diet. I find in hospital practice that the admirable rule laid down for feeding in whooping-cough, namely, to feed immediately after a paroxysm so as to allow time for digestion before the next spasm, is impossible to carry out for all cases, unless a very

large nursing staff is employed. When a fairly liberal diet, including a considerable proportion of cooked food, is given, such a method is inapplicable to a large number of patients. Even if an otherwise healthy whooping-cough patient vomits the greater part of his dinner at once, he is usually perfectly ready to take it again and retain it, if he is given the chance, as he should be. All children, then, who are able to be out of bed, and who are over two years of age, are allowed as in health ordinary meals suitable to their age, consisting usually of white fish, occasionally minced meat, potatoes, eggs, milk puddings, oat-flour porridge, and bread and butter. As long as the patient does not appear to be losing weight, and if the paroxysms are not unduly frequent or severe, the fact that the food is to some extent vomited is a matter of small importance. In private practice, where it may be possible for a nurse to devote her whole time to one or two patients, even in sthenic cases the meals may be so arranged as to be given just after a whoop, as the interval between the paroxysms is often fairly definite. In this way some loss by vomiting may be avoided.

If, however, the case is more severe, the greatest care must be taken. It may be found, for instance, that the paroxysms are exceptionally frequent, and that a large proportion of the food ingested is vomited. Or the patient may appear to be losing weight, and, perhaps, is not properly assimilating the food which he retains. In such cases, and in the prolonged bronchopneumonias which are so frequently the cause of death in this disease, it is wiser to restrict the food to fluids, and to give small quantities at frequent intervals, if possible just after the whoop. A certain amount of this will be usually digested, even if the vomiting with the next paroxysm is severe. I generally feed such patients on milk, often given with lime-water to correct any gastric acidity, or on small amounts of meat juices or extracts. Malt foods appear to be sometimes of advantage, and most children take Benger's food and other similar preparations well. In bad cases the milk should be peptonized, and albumin water may, with advantage, be added to it. In less severe cases, milk puddings and starchy foods may be given, but, as Eustace Smith points out, anything which is liable to cause fermentation or acidity is better avoided. Under this heading he classes farinaceous puddings, jam, and fruit, all of which are harmless enough in older children and mild cases, but are certainly better dispensed with in the class of case at present under consideration. It must be remembered that gastric disturbance may do much to curtail the short snatches of sleep which such patients enjoy between their spasms, and so increases the nervous irritation which is so marked a feature in a bad case of whooping-cough.

Individual cases may present marked differences. Trousseau held that

solid food is better taken than liquid, and occasionally, even in severe cases, this dictum may be remembered with advantage. I seldom, however, allow solids in a really serious case, whether pyrexia is present or not. In cases of moderate severity, if solid food seems to make the patient worse, soft solids may be used, such as porridge, rusks or sponge biscuits soaked in milk, bread and milk, and so on. Dry solid food, which may leave crumbs in the fauces, is very apt to excite the cough. Again, in the worst cases, if milk is not tolerated, it is always worth while to make a trial of whey, which is often most useful for infants.

If the patient refuses food altogether, everything should be done to persuade him to eat, and I am often willing to tempt such a child by allowing him to eat anything in the way of food that he fancies, even if the article demanded does not appear very suitable. Rectal feeding is so unsatisfactory that we should try everything possible before resorting to it. Occasionally, however, it is our only resource. As regards the dieting of bronchopneumonia, which should, generally speaking, be fluid, I have noticed, as after measles, that treating the patients in the open air makes them easier to feed, a remark which, after all, applies to all cases of whooping-cough. When diarrhoea is present, the addition of lime-water to the milk, and the use of raw meat juice or bovine, with appropriate medicinal treatment, is indicated.

Stimulation is seldom necessary except in complicated cases. Occasionally, however, there is great exhaustion after the whoop, and some children are better for an occasional dose of a half-teaspoonful of whisky or a little white wine whey.

Drug treatment. An enormous number of drugs have been employed in whooping-cough, their very number witnessing to their frequent inefficacy. They are chiefly tonic, expectorant, or antispasmodic. It is unnecessary to enumerate them. I have tried very many without much effect either on the length of the disease or on the severity of the paroxysms. There is a good deal of sound common sense in the saying of the South German peasant, quoted by Sticker, that whooping-cough 'continues until it stops'. And there is also much to be said for the late Professor Osler's prescription, 'six weeks and a good big bottle of paregoric', regarding which I should be inclined to lay special emphasis on the 'six weeks'.

Quinine has long enjoyed a reputation in the treatment of whooping-cough, and is particularly effective towards the end of the paroxysmal stage, when it may be given in moderate doses, one grain for each year of the child's life, twice daily. Its main action is probably tonic. During the height of the illness I have not seen it exercise any particular influence on the

number or character of the paroxysms, although I recently made a trial of its hypodermic use. It is, therefore, better to preserve it for the later stages of the disease. Iron tonics are better avoided unless there is no gastric disability. During both the catarrhal and paroxysmal stages a mild expectorant often helps to make the cough easier. For this purpose I prefer ipecacuanha wine in doses not exceeding 5 minims every four hours, and given just after a whoop. Of *antispasmodic drugs*, which I usually reserve for bad cases, belladonna has given me by far the best results. But, if it is to have any effect on the severity of the spasms, it must be given to the full physiological extent, till the pupils are widely dilated. I usually start with 3 minims of the tincture four-hourly and add a minim daily, till doses of even 10 or 12 minims are reached. Children take the drug extraordinarily well. Not infrequently, however, rashes will follow its use. I cannot say that I have much faith in belladonna reducing the number of the paroxysms, but I am convinced that in many instances their severity is much diminished by its employment. Bromides are occasionally useful, the sodium or ammonium salts being preferable. They may be combined with the belladonna in some cases with great advantage, but it is well to give only moderate doses and to avoid depressing the patient by their prolonged use. Often when the paroxysms do not appear favourably affected by one drug they may yield somewhat to another. Butyl chloral hydrate is recommended by Eustace Smith in doses of one grain every two, four, or six hours, according to the age of the child. I have seen it successful when belladonna has failed, but it, like other remedies, is often disappointing. For sthenic cases, antipyrin is as useful an antispasmodic as any, but I do not regard it as a suitable drug for the weakly children who compose the great majority of my hospital patients. On the other hand, I believe that it has a real influence on the paroxysms, and I always depend upon it for adults. I discarded the use of bromoform after a fair trial, not on account of its alleged risks, but because it gave me no good results, although in the hands of others it appears to have met with considerable success. It is used in doses of 1 to 3 minims, made up with water and syrup of oranges. The bottle should be well shaken before use, otherwise the bromoform is apt to sink to the bottom, causing the last few doses to have poisonous effects. Other drugs which may occasionally be used are hyposcyamus, heroin, and opium, the latter of which may be prescribed in the form of paregoric or Dover's powder; and by some is combined with belladonna or atropine.

Some physicians have suggested that *local treatment* be applied to the larynx. I have never seen any real advantage follow the inhalation of

medicated vapours. I made a trial of the application of resorcin, 2 per cent. solution, to the vocal cords, but was not long in dismissing it as useless.

In very severe paroxysms with prolonged spasm of the cords, Smith says that instant relaxation follows the putting of the child's hands into cold water, a method of which I have no experience, but which from its harmlessness and simplicity well deserves a trial. O'Dwyer recommended intubation for severe cases with much spasm. It is obvious that, with a tube *in situ*, the inhalation after the explosive coughs is made without difficulty, and the child suffers proportionately less. It is only, however, in very bad cases I consider such interference justified, and all that can be expected from it is to give one or two days' rest to the patient, as it would be unwise to leave a tube in long. After the withdrawal of the tube the disease continues to run its natural course. Although I have often been prepared to intubate in case of need, I only recollect doing so on one occasion.

Many believe in the advantage of a firm bandage round the abdomen and lower ribs to give support during the paroxysm. This should be made of some elastic material very tightly applied, and prevented from slipping by braces fixed to it and passed over the shoulders as suggested by Kilmer. There is no doubt that such fixation gives considerable relief to the patient and, I think, also diminishes the vomiting. I frequently make use of a broad bandage for this purpose.

To influence the neurotic element of the disease Zangger speaks highly of hydrotherapeutic measures. He advises the use of the tepid, 54° to 60° F., pack, a sheet being well wrung out, wrapped round the patient, and covered with a blanket secured with safety pins. The patient may be left from 10 p.m. till morning in one of these packs, which must be applied loosely enough to enable him to sit up during a paroxysm, and the sedative action is very marked. I am experimenting with this treatment, but have not had sufficient experience of it to justify a definite opinion of its value.

Weill considers that frequent inhalations of oxygen are efficacious in reducing the violence of the paroxysms. I have from time to time made use of this method in severe cases of broncho-pneumonia, but cannot say that I have much faith in it. It is possible, however, that I have had recourse to it too late.

In *convalescence*, iron tonics, malt foods, or cod-liver oil should be given, and much good may be effected by a complete change of air and scene.

Specific Therapy. Although we may agree with Williams that the evidence in favour of Bordet's bacillus being definitely the cause of whooping-

cough is not quite complete, it appears to be sufficient to justify attempts at both serum and vaccine treatment, and much work has been done especially in connexion with the latter method. As regards *serum* treatment Klimenko succeeded in preparing a serum with which he claims to have treated thirty-five children with a certain degree of success in ameliorating the number and violence of the paroxysms. But his results do not appear to be very striking.

As regards treatment with *vaccines* my own experience some years ago was not very favourable; that is to say, the cases did not seem to be affected one way or the other. But the commercial vaccines employed were given in doses which, from the experience of recent workers, were too small to be of any value. I am prepared, then, to approach the subject with an open mind, though a study of the literature seems to point to vaccines being of more value for prophylactic than for therapeutic purposes.

Luttinger in an analysis of 952 cases treated with vaccines comes to the conclusion that the average duration of the paroxysmal stage is shortened. On the other hand, Von Sholly, Blum, and Smith found they got quite as good results by the injection of influenza vaccine, and even of a solution of milk and water, as they did when the specific vaccine was used. These observers justly emphasize the great difficulty of estimating the value of any method of treatment in an illness as uncertain in its duration and irregular in its course as whooping-cough. Graham, Huenekens, Hartshorn and Moeller, Fischer, Shaw, and Bloom all believe that there is more or less advantage in using vaccines therapeutically. Huenekens recommends them in particular for the catarrhal stage. On the other hand, Hess, Barenberg, and Foote seem to doubt if they have any real therapeutic effect.

As regards *dosage* and *interval* the best results seem to have been obtained by the advocates of the large dose. The New York Health Department suggests 500 million, 1,000 million, and 2,000 million as doses. Luttinger doubles these amounts and Fischer recommends 1,000, 2,000, and 5,000 millions, the injections being given every other day. Bloom, who like many others uses a mixed vaccine, also favours the large dose, starting with 5,000 millions and repeating or increasing this amount every second day up to 7,000 millions, four or five doses being usually sufficient. He recommends

Bordet-Gengou bacillus	.	.	.	1,000 millions
Staphylococcus Aureus	.	.	.	500 „
Micrococcus Catarrhalis	.	.	.	40 „
Bacillus Influenzæ	.	.	.	160 „
Streptococcus Pyogenes	.	.	.	100 „

and considers that such a mixture, used in the large doses recommended above, minimizes the loss of weight, reduces the duration and decreases the intensity of the paroxysms, and also limits the mortality.

It may be added that these large doses appear quite safe and do not cause any unpleasant reaction. It would seem reasonable to employ them, therefore, in any further work undertaken to establish the value of this method of treatment. Prophylactic vaccines will be considered below.

Treatment of complications. As regards *broncho-pneumonia*, I used to treat the patients on the lines which are, even now, most in favour, with a medicated vapour, usually creasote, and the steam tent. The death-rate under those conditions was, in my experience, appalling, often exceeding 70 per cent. The mortality was largely due to want of proper sleep and rest, to loss of appetite and difficulty in administering adequate nourishment, and to supervening tuberculosis. It was the possibility of combating these three conditions, particularly the last, which encouraged me in the face of a good deal of criticism to treat these patients in the open air, so far as circumstances permitted, and the improvement in my results was so astonishing that for the last eighteen years I have continued this method, the success of which led me to give also uncomplicated cases the advantages of free ventilation. To mention only my original statistics relating to this point, of a series of seventy-four cases treated indoors entirely, and in a warm atmosphere, fifty-one, or 66·9 per cent., terminated fatally, while of seventy-six patients treated partly or entirely under open-air conditions, twenty-four, or 31·5 per cent., died. Since then the mortality has been as low as twenty-six, and as high as forty, in different years, much depending doubtless on the prevailing climatic conditions, the fatality being greatest in wet seasons, during which, it may be remarked, the patients cannot be carried out into the gardens. The value of open air in acute pulmonary conditions has been emphasized by Northrup. I consider that there is no doubt that the patients so treated eat better, sleep better, and develop tubercular sequelæ less frequently, and that all these advantages are directly reflected in the lowered death-rate. The only contra-indication to open-air treatment is the occurrence of laryngitis.

In broncho-pneumonia the patient's strength must be supported by appropriate stimulation. Alcohol is usually necessary, and whisky in half-drachm doses at suitable intervals is in most cases well taken. White wine whey is also a useful preparation, and may be made by adding a wine-glassful of sherry to half a pint of warmed milk, and then straining. Strychnine is valuable, but it is apt to increase the nervous excitability too much

to make it a suitable drug to use in all cases, or to continue for long. *Strophanthus* and *digitalis* occasionally give good results. The chest should be wrapped in a Gamgee jacket and well rubbed with stimulating oils. I have occasionally seen improvement follow the application of leeches to patients in whom cyanosis was very pronounced.

Convulsions are so very fatal that treatment is often of no avail. Chloral and bromide may be administered by the rectum, when fits have once occurred, to prevent their recurrence. For the fit itself I usually try a hot bath with mustard, or a hot pack. In very prolonged convulsions a whiff of chloroform may give relief. Recently we have been attempting to relieve the condition by lumbar puncture. Sometimes, when much fluid is withdrawn under high pressure, immediate amelioration follows, but in other patients the method is useless, and in any case it does not prevent the recurrence of the convulsions.

For persistent *vomiting* I am usually content to modify the diet and depend upon rectal feeding. Goodall speaks favourably of hydrochlorate of cocaine in doses up to $\frac{1}{4}$ grain thrice daily. Latterly I have been using adrenalin, and am inclined to believe it is of service. For *diarrhœa* a dose or two of grey powder, and the washing out of the large intestine with an irrigation, will be found useful.

PROPHYLAXIS. The isolation, during times of epidemic, of children suffering from a febrile catarrh would appear the most satisfactory method. In institutions the question of a differential leucocyte count might be considered with advantage. Although in the paroxysmal stage there is but little infectivity, it is generally advisable to isolate patients for six weeks from the commencement of the whoops, or less if the paroxysms stop before that date. The patient should be taught to use a spittoon, and all sputum should be disinfected. It is a good precaution to thoroughly disinfect the rooms which have been occupied by a patient, and the same remark applies to his clothes.

It is to be hoped that compulsory notification will enable the authorities to get a better control of this very serious disease. As an American physician has remarked, a child who dies of whooping-cough is just as dead as if he had died of plague, and yet the enormous mortality of whooping-cough is regarded quite tranquilly by the public and the profession. It appears that *immunization* by vaccines offers a distinct prospect of improvement. It is only, however, since the use of large doses was introduced that favourable results have been obtained, and now most workers with vaccines seem to agree that the prophylactic value is considerable. Huenekens has succeeded in demonstrating antibodies in the blood of inoculated

children. He considers that the vaccine should be freshly prepared and that no preservative should be added. He recommends 1,000, 1,500, and 2,000 million doses on alternate days. Bloom prefers 5,000 millions repeated three times and states that, so far, vaccination has protected for two years all those inoculated with this dose. It is most desirable that an exhaustive trial of this method of protection should be made in institutions in this country.

CHAPTER XIII

MUMPS

Etiology.	Localization of the Inflammation : Orchitis,
Infection and Dissemination.	Pancreatitis, Meningitis.
Morbid Anatomy.	The Blood in Mumps.
Period of Incubation.	Complications.
Period of Invasion.	Diagnosis.
Course of the illness: the parotid swelling,	Prognosis.
general symptoms.	Treatment.
	Prophylaxis.

SYNONYMS—Specific Parotitis, Epidemic Parotitis. *French*, Oreillons. *German*, Ziegenpeter.

ETIOLOGY. It may be assumed that the cause of mumps is a specific micro-organism. Recent work tends to show that it will prove to be ultra-microscopic, and we need not consider seriously the cocci described by Laveran and Catrin and by Teissier. Gordon has satisfactorily proved that the virus occurs in the saliva and passes through a Berkefeld filter, and, when injected into the brain of the monkey, is capable of producing a lymphocytic meningitis, together with a hyperæmia of the central nervous system. Acute interstitial parotitis may be produced if the animal survives sufficiently long. Nicolle and Conseil, using fluid obtained by parotid puncture for intraperitoneal injections, caused, after a suggestive incubation period of from nineteen to thirty days, a febrile illness in three bonnet monkeys, in one of which parotid swelling also developed. Injections of blood from human patients gave no result. Wollstein, who, like Gordon, used filtered saliva, also comes to the conclusion that the virus is filterable. She injected it into the parotids and testicles of half-grown cats and found that pyrexia and leucocytosis followed almost immediately, and that there also was a reaction in the uninoculated salivary glands. The pathological findings were not unlike those described in mumps. She failed to demonstrate the presence of the virus in the cerebrospinal fluid, but claims to have detected it in the blood. An interesting feature of her experiments was the fact that, if the saliva was mixed with the serum of a cat which had survived the injections, no resulting reaction followed.

Differences of climate appear to have little influence on the occurrence of mumps, which has been observed all over the world. *Season* does not appear to be of much importance, although it is probable that most epidemics occur in the spring or autumn, and it has been observed, I think justly, that the disease seldom appears during the summer term of schools. As regards *age* the great majority of persons affected appear to be between the ages of five and fifteen years. Infants very rarely suffer from mumps, and it is exceptional to find it in persons of over forty years of age. It is a disease of schools and also of barracks, and has recently been very common among both soldiers and sailors during the war.

INFECTION AND DISSEMINATION. The virus no doubt lies in the buccal and nasal cavities of the patients, and is usually transmitted by 'droplet' infection. While it can undoubtedly be carried by third persons, its infectivity, except by direct contact, is not high. The germs contained in the secretions are probably quickly destroyed by exposure to air. I have, for instance, found it most exceptional for a nurse to carry the infection from one patient to another so long as they are nursed in separate rooms. The disease, however, will readily spread in a hospital ward, the patients in the adjoining beds being the first to be affected.

MORBID ANATOMY. As might be expected in a disease of which the prognosis is uniformly good, little work has been done which throws light on the exact character of the enlargement affecting the salivary glands. Some regard it as a mere hyperæmia. The parenchyma of the gland appears to be entirely unaffected and free from any inflammatory process. The interstitial tissue of the gland itself is also said not to suffer, and the enlargement would seem rather to depend on the swelling of the connective tissue surrounding it, and of the lymphatic glands in its neighbourhood. In cases of atrophy of the testicle the parenchyma is involved and function is destroyed.

INCUBATION. The period of incubation is somewhat long, and the usual limits are twelve to twenty-six days. In the majority of cases the disease takes from seventeen to twenty-one days to develop. For practical purposes it may be assumed that a person exposed is safe when twenty-six days have elapsed from the date of the last exposure.

INVASION. As a rule the swelling of the parotid is the first symptom to attract attention. A prodromal period, more or less well marked, may nevertheless be often noticed, and this sometimes lasts as long as two or three days. The most frequent symptoms are malaise, chilliness, headache, and fever, which occasionally may be severe. Epistaxis is not infrequently noted, and earache, affecting one or both sides, should be regarded with great suspicion if it occurs in a person recently exposed to infection. The

patient may also suffer from sore throat of varying severity. In rare instances the onset of the disease is heralded by severe meningitic symptoms.

COURSE. With the appearance of the parotid swelling the disease may be said to have entered on the stage of advance. This swelling is first observed below the ear, filling up the hollow between the mastoid process and the ascending ramus of the lower jaw. In very mild cases this enlargement of the parotid may be so slight as to be hardly recognizable, but as a rule it is exceedingly obvious. It is usually for the first day or two unilateral, although occasionally both parotids are swollen from the commencement of the illness. In any case the second parotid rarely escapes, its enlargement commencing within two or three days of the onset. The swelling on each side spreads downwards and sometimes even reaches the clavicle. The submaxillary and sublingual glands may or may not become involved, and the cervical lymphatic glands possibly also suffer. The general effect of this swelling is to give a most ridiculous aspect to the patient, especially if the inflammatory process spreads from each side till it meets under the chin. Occasionally there is also oedema in the upper part of the face, chiefly to be noticed in the eyelids. The skin over the swelling is tense and smooth, and, as a rule, not reddened. There is tenderness on pressure, but not much pain, except in movement of the jaws. In fact mastication is sometimes rendered almost impossible by the stiffness and tenderness of the face, and laughing or talking causes very great discomfort to the patient. Occasionally a slight degree of trismus is present, the teeth being clenched as if from some reflex action.

It is probable that if the throat was examined in every case, a large proportion of the patients would show varying degrees of tonsillitis. A complete examination of the mouth and throat is, however, rendered very difficult by the pain which it occasions, and is of no assistance in facilitating diagnosis, as nothing characteristic can be seen before the parotid swelling occurs. It is stated, however, that the mucous membrane is acutely congested in the neighbourhood of the orifice of Stenson's duct, which becomes readily visible at the level of the crown of the second upper molar on the affected side. I have, nevertheless, frequently failed to notice this congestion. The effect of the inflammation upon the excretion of saliva varies. While in some patients the mouth is dry, in others the amount of saliva seems to be markedly increased. Comby has found that its reaction is more often acid than neutral.

The resolution of the parotid swelling takes place in most instances very rapidly. The gland usually regains its normal size in a week or ten days from the commencement of the process. There may, however, be some delay before the parotid of the opposite side becomes affected, and relapses

occasionally occur. Resolution is quicker in children than in adults ; as a rule, indeed, the latter are liable to suffer more severely during the whole course of the disease. No thickening or induration is left after the swelling subsides. As regards suppuration, some authors have stated that it never occurs. This is, however, an error. I have seen suppuration of both parotids in an adult, and while all agree that this complication is most rare, especially in children, nevertheless it may have to be reckoned with. When suppuration does occur it no doubt depends on a secondary infection by pyogenic organisms.

The *fever* may continue as long as the glands remain enlarged, and, in adults especially, is occasionally high. But some patients go through their whole illness without a rise of temperature.

OTHER LOCALIZATIONS OF THE INFLAMMATION. Occasionally a case of true mumps is seen in which the parotid altogether escapes, the salivary gland primarily affected being the submaxillary. Such cases are easy to diagnose during an epidemic, but otherwise are likely to be missed. In some instances the difficulty is removed by the parotid becoming secondarily involved.

The most interesting feature, however, of this obscure infection is unquestionably its tendency to cause inflammation in the sexual glands. Of these inflammations **orchitis** is by far the most common. This complication is not observed before puberty, except in rare instances. It is, however, frequently met with in adolescents, and, according to the French authors, appears in one-third of the cases when an outbreak occurs among soldiers in barracks. I have seen it affect nearly as high a proportion of the older boys of an industrial school who were sent into hospital suffering from mumps. In a recent series of 243 males above the age of puberty, chiefly British and American naval ratings, 42 or 17·2 per cent. developed orchitis. Through the kindness of my former assistant, Captain M^cMichael, I have received a note of the complications of 345 soldiers treated in a general hospital in France, and in this series also a very similar percentage, 18·8, occurred. In my own series the right testicle only was affected in 15 cases, the left in 10, and both in 6, the location of the remaining 11 not having been noted. It is generally agreed that, if the patients are confined absolutely to bed for the first eight days, the incidence of the complication is much less than when they are permitted to rise at an earlier date, but as none of our own patients are allowed up before the ninth day it will be seen that rest cannot be expected to prevent orchitis, which occurs frequently in spite of all precautions. As regards the day of onset, 27 of my cases occurred on or before the ninth day, the earliest being noted on the third and the greatest

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MUMPS.

The parotid glands have been painted with iodine to emphasise their contour.

number, seven, on the seventh day. Twelve cases occurred after the ninth day, of which 10 appeared from the twelfth to the fifteenth day inclusive. In one patient the orchitis was as late as the twenty-first day. While, then, the onset is very variable, the most common time seems to be towards the end of the first week and usually coincides with the subsidence of the parotid symptoms, and it has, therefore, been described as an instance of *metastasis*. Probably, however, its occurrence merely points to the affection of another organ by the virus of the disease. Orchitis may occur as the primary, or even the only, manifestation of mumps; in some outbreaks, indeed, cases in which the testicle is the only gland affected are comparatively common.

Orchitis is often attended by severe constitutional symptoms. These are frequently out of all proportion to the amount of local inflammation and to the pain which it may cause. Some patients may complain of pain but little, although the gland is swollen and tender. In others the pain may be very severe, and the tenderness exquisite. But in the majority the temperature rises suddenly and rapidly, sometimes attaining so high a level as 104° (see Fig. 56). Shivering, vomiting, delirium, and sometimes even meningitis may accompany the onset. Occasionally the patient is pale and collapsed, and presents an abdominal facies. The affected testicle may become much enlarged, and the rapidity with which it increases in size is often striking. Both the body of the testicle and the epididymis may suffer. There is some difference of opinion as to which part is affected first. I am not able to throw any light on this point, but I have not noticed a case in which the epididymis alone was affected, and in many the body of the organ seemed to be the only part attacked. Feiling holds that the epididymis suffers first and that the body is affected later, and quotes Chauvin, who in a series of cases found the epididymis and body both involved in fifteen instances, the epididymis alone in two, the body alone in three, and the vasa deferentia alone in three. In some instances a slight urethral discharge accompanies the swelling. The process, fortunately, lasts only a short time in the majority of cases, the inflammation subsiding in from three days to a week, the subsidence being as rapid as the enlargement. The opposite testicle, however, may become involved, and, if so, the swelling and acute symptoms of onset usually appear on the third or fourth day after the first attack of orchitis. The real seriousness of the condition lies in the fact that it is not infrequently followed by atrophy of the gland.

Of the other so-called metastases we may note that the *ovaries* are occasionally found to be tender. It is unusual, however, for any enlargement to be made out in this situation. The mammary gland may also suffer, and *mastitis* has been known to occur even in boys. The *lachrymal gland* is said

to be sometimes affected, and a case has been reported in which the *thyroid* became extremely enlarged. *Vulvitis* is also seen in rare instances.

Recently much attention has been drawn to **pancreatitis**, which, in some outbreaks, appears to be relatively common. Edgcombe has noticed it in no less than five cases out of thirty-three boys suffering from mumps. The main features common to all these were rapid subsidence of the parotid swelling, vomiting, pain and tenderness in the epigastrium, and constipation.

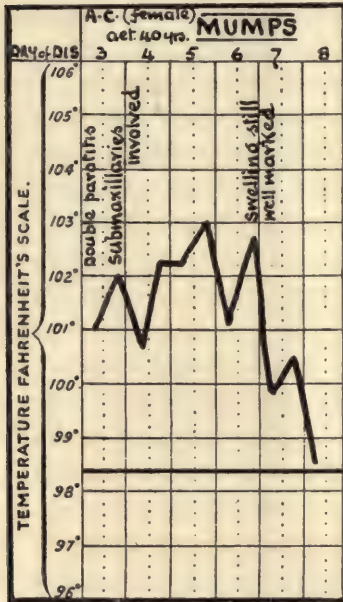


FIG. 55. A sharp case of mumps in a female adult. Considerable pyrexia.

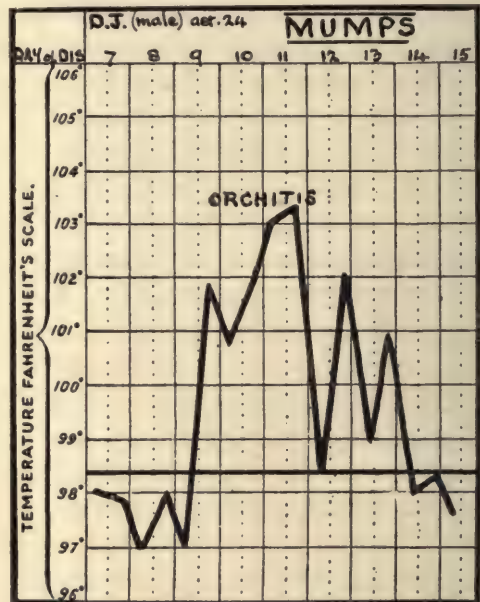


FIG. 56. Illustrating the sharp fever often observed in orchitis. Patient was admitted with the parotid swelling almost subsided. On the ninth day the right testicle commenced to swell. It was back to its normal size by the fifteenth day.

In two cases a tender transverse swelling could be palpated. In one, the pancreatic reaction was found to be present in the urine. Gordon Sharp's experience is also interesting. In an outbreak observed by him, pancreatitis appeared very frequently, and in one instance preceded the appearance of the parotid swelling. He emphasizes the alarming nature often presented by the abdominal symptoms. Collapse, intense vomiting, occasionally of blood, and marked pain in the epigastrium and left hypochondrium characterized his cases. The complication sometimes appeared late in convalescence. Other observers report similar cases, and cases of polyuria

and glycosuria have been described. In one case an attack of diabetes mellitus three years later was regarded as a late sequel of mumps, and this disease has also appeared in the course of a case of mumps with no obvious abdominal symptoms. Pancreatitis, then, must be regarded as a recognized complication of the disease, but it is in most outbreaks extremely rare. In a very widespread epidemic in Edinburgh in 1909 no case came under my own observation or that of the very large number of medical practitioners whom I had asked to look out for it. Capitan in a recent series of 700 military cases observed no instance of it, and in my own extensive experience I have only seen one certain example.

The association of mumps with **meningitis** has been noted for many years, and since the introduction of lumbar puncture evidence of a more definite character has been at our disposal. I have only seen one case with decided meningeal symptoms, which ushered in the disease and subsided rapidly with the appearance of the parotid swelling, and in that instance the suggestion was rather one of meningism than of actual meningitis. But there are many undoubted cases reported in the literature in which lumbar puncture revealed excessive numbers of lymphocytes in the cerebrospinal fluid, and in some fatal cases definite evidence of meningitis has been found post mortem. Death is none the less unusual, the symptoms ordinarily subsiding rapidly. The condition appears usually to occur at the height of the illness, and comparatively frequently with the onset of orchitis, but occasionally it precedes the parotid swelling. It may be mentioned that a lymphocytosis is observed in the cerebrospinal fluid of cases of mumps even when no meningeal symptoms are present.

THE BLOOD IN MUMPS. A considerable amount of attention has been recently paid to this question. Feiling, who examined forty-two cases, concludes that there is a slight increase in the total number of leucocytes, and that a lymphocytosis, both relative and absolute, is present on the first day and persists at least fourteen days, the average lymphocyte percentage being 48. This lymphocytosis, which does not appear to be disturbed even by the appearance of such a complication as orchitis, seems to have been noted by all workers on the subject. Lehnndorff, however, and also Marcovici, considers that the total number of leucocytes remains normal. Both note that at first the eosinophiles are diminished or normal, and the latter states that after the tenth day there is a post-infective eosinophilia. All agree that diagnosis is much assisted by blood examination.

COMPLICATIONS. These are met with very rarely, but appear to be very varied in character. The heart occasionally suffers, and instances of bradycardia, attributed to glandular pressure on the vagus, endocarditis, and

myocarditis have been reported. Phlebitis is also stated to be occasionally associated with mumps. Arthritis is sometimes seen, and may prolong the convalescence of the patient. Various forms of erythema have been described as occurring during the course of the disease. Albuminuria occasionally occurs, but is in my experience uncommon, and is usually transient. I have never observed a case of *nephritis*, but there appear to be a fair number of cases reported in the literature, and in Captain McMichael's series of 345 cases no less than five, one of which was fatal, are noted. It is possible, however, that other factors than mumps may have been responsible in a hospital not far from the trenches. A great variety of *nervous complications* have been reported. Facial paralysis due to direct pressure of the swollen parotid or to toxic neuritis, paralysis of other cranial nerves, and peripheral neuritis are among the number. Aphasia and myelitis have also been noticed. Mania and melancholia may follow an attack.

More important are the *ear complications*. Deafness may follow middle ear disease following infection with pyogenic organisms by way of the Eustachian tube, and in some outbreaks otorrhœa, which has on the whole been rare in my own experience, is relatively common, ten out of McMichael's 345 cases presenting this complication. More specific and characteristic of the disease is damage to the labyrinth and total and permanent nerve deafness, which appears to have occurred in four of McMichael's series. The deafness, which may be preceded by tinnitus and vertigo, usually becomes evident within four days of the onset of the illness and has been attributed by some writers to basal meningitis.

Of *eye complications* optic neuritis is perhaps the most frequent. Paralysis of accommodation and toxic amblyopia have also been observed. Iridocyclitis has been known to both precede the parotid swelling and to follow it.

DIAGNOSIS. During an epidemic this should present little or no difficulty. The sudden appearance of a parotid swelling in a person previously quite healthy should be quite sufficient. In examining the patient it is advisable to get him in such a position that a good view is obtained of the outline of the face and neck, so that both sides may be seen at the same moment and accurately compared. In a mild case there may at first be little more than a slight fullness in the hollow below the ear on one side of the face. The tendency of the inflammation to become bilateral should quickly clear up a doubtful case, the parotitis which occurs in the acute infections being usually limited to one side. The difficulty in opening the mouth and the pain which it occasions distinguishes the disease from ordinary glandular enlargements which may simulate it, but it must be recollected that, in mild cases, the mouth can be opened without pain. Mirchamp has

stated that if vinegar is applied to the tongue a painful reflex secretion of saliva occurs in the affected gland. I have made a fair trial of this test in a good number of true cases, but have always found it quite negative, although it has been stated that it is useful in distinguishing the orchitis of mumps even when that condition is the only sign of the disease. The recognition of mumps when it primarily affects the submaxillary or sublingual glands is extremely difficult. In such a case the sudden appearance of the swelling, the absence of anything in the mouth or elsewhere to account for it, and the presence of an epidemic are the most important points in favour of a positive diagnosis.

It must be remembered that parotid swellings are liable to occur in typhus and enteric fevers and in various general septic conditions. Usually in these cases the enlargement, as has been said above, is unilateral. It is slower to develop and as a rule ends by suppuration. The great swelling which may occur at the angle of the jaw in cases of scarlatina or diphtheria is occasionally mistaken for mumps. Some of the deaths registered as resulting from mumps are indeed not improbably due to diphtheria, and when we read of convalescents from mumps suffering from paralysis of accommodation, peripheral neuritis, and other symptoms which we are more accustomed to associate with diphtheria, we are at liberty to suppose that the two diseases are occasionally confused. It is rare, however, for a diphtheria patient to have much difficulty in opening his mouth, and in any case an examination of the fauces is all that is required. Nevertheless, I have had several severe cases of diphtheria sent into the hospital as mumps. Parotid swellings may also be met with in cases of lead poisoning and in iodism. In these conditions, however, the development of the swelling is slow and gradual.

While the diagnosis of mumps, even when the swelling remains unilateral, is easy during an epidemic, the value of a differential leucocyte count should not be forgotten. A definite lymphocytosis serves to distinguish the condition from a swelling of septic origin, and this method of diagnosis, which appears to be equally reliable in cases of orchitis, should be particularly useful in those cases in which the testicle is the only gland affected by the virus. The lymphocytosis of the spinal fluid, moreover, may assist diagnosis, and in cases of suspected malingering, such as have been reported among Moroccan soldiers who acquired the trick of inflating their parotid glands by forcible blowing with the mouth shut or into a bottle, lumbar puncture would be a very justifiable procedure.

PROGNOSIS. Children for the most part recover quickly and without complications. In adolescents and adults resolution may take somewhat longer, and the patient may complain of lassitude and want of strength for

some weeks. The uncertain part of the prognosis concerns the future of the testicle rather than the life of the patient, especially when adolescents are concerned. We have seen that orchitis sometimes complicates one-third of the cases, and it may be added that in some outbreaks more than half the cases of orchitis progress to atrophy. As both glands are not infrequently affected, it is obvious that the results of this complication may be very serious. Otherwise the prognosis may be said to be uniformly good, except in cases with actual meningitis, which are fortunately very rare. Toxic neuritis of the cranial nerves is usually short-lived. Nerve deafness, on the other hand, usually remains permanent.

TREATMENT. It is, of course, necessary during the febrile period to keep the patient in bed, and it is desirable, even in mild cases, that this rest should be prolonged for at least ten days. All authorities agree that orchitis is much more frequent in patients who have been allowed to get up too soon. As regards general treatment, the patient is often the better for a mild purgative, say 3 grains of calomel, at the commencement of the disease. The food should be fluid or semi-fluid, and care should be taken to see that the patient takes sufficient, as the difficulty of opening the mouth often renders him reluctant to eat. It is probably an advantage to wash out the mouth frequently with weak antiseptics. A certain amount of stomatitis is nearly always present, and the careful toilet of the mouth may be of service in preventing the infection of the middle ear by way of the Eustachian tubes. It should also reduce the chances of suppuration of the parotid to an absolute minimum, and, as Comby suggests, may even lessen the probability of metastases. Listerine, a dessert-spoonful in a small tumbler of hot water, makes an agreeable mouth-wash, or in younger children can be used as an irrigation.

As regards the local condition, all that can be attempted is palliation. Simple hot fomentations, frequently renewed, are probably as useful as any other form of application. Or cotton-wool, covered with oiled silk, may be placed on the swollen glands and a bandage fixed over all. Some patients appear to get relief from the use of ointments. Belladonna ointment may be applied on a piece of lint, or a preparation of one part of guaiacol in twenty of a mixture of lanoline and vaseline can be used. Orchitis can be treated on similar lines. The parts should, of course, be well supported with cotton-wool and some suitable form of suspensory bandage.

Much cannot be expected from any form of treatment in cases of deafness. Injections of pilocarpine are recommended and should be started at once, but it is admitted that even the early employment of the drug may be quite ineffective. Hubbard, who considers that the serious effects of the labyrinthitis are chiefly due to the fact that there is no room for

inflammatory products within the rigid walls of the labyrinth, suggests that lumbar puncture, by lowering subarachnoid tension, might reduce the pressure of the perilymph and give more encouraging results.

PROPHYLAXIS. The *isolation* period usually recommended is three weeks, and there is much to be said for detaining male patients for this time in view of the fact that the onset of orchitis is occasionally late. But in dealing with women and children my rule for many years has been a minimum isolation of a fortnight and the detention of the patient for one full week after the subsidence of all visible swelling. The latter recommendation implies that certain cases with prolonged parotid swelling are not infrequently isolated for three weeks or longer. On no occasion has infection followed the discharge of patients treated in this manner. The *quarantine* period should be not less than 26 days, and, as has been already suggested for mild diseases with long incubations, such as rubella and chicken-pox, it seems reasonable that for 10 days after the first exposure a child might quite safely be allowed to attend school. As second attacks are very unusual, children who have already had the disease should be excused quarantine altogether.

Mumps is apparently infectious from the moment of the first symptom, possibly, indeed, a short time before anything wrong is noticed. In an outbreak in a school it is well to take the temperature of all exposed twice daily, and to isolate promptly any contact who shows the slightest sign of malaise or even slight pyrexia. Headache and earache should be regarded as suspicious symptoms. With care much may be done to limit the spread of infection. It is interesting to note that some writers seriously question the advisability of endeavouring to protect children from exposure to the disease. From their point of view it is better to contract the illness before puberty, and to get it safely over, than to run the risk of taking it later on in life and of perhaps suffering from atrophy of both testicles. Personally I cannot regard it as a justifiable procedure to expose any one wilfully to any infectious disease, however trivial. Moreover, experience teaches us that orchitis is seldom serious in patients who have been kept carefully in bed, and its risks have probably been overestimated. On the other hand, it seems unnecessary to go so far as to attempt to protect children by the inoculation of convalescent or immune blood. Experiments carried out by Hess, who has injected 'whole blood' with this object, suggest that the method is quite probably efficacious. The virus is probably short lived, and terminal *disinfection* does not seem to be very important although I am accustomed to practise it in hospital.

Note.—A very valuable bibliography of recent work on Mumps is attached to a critical review of the whole subject by Feiling in the *Quarterly Journal of Medicine*, April 1915.

CHAPTER XIV

CEREBRO-SPINAL MENINGITIS

Etiology : predisposing factors.

Infection and Dissemination : Carriers : path of infection.

Morbid Anatomy.

Bacteriology : Types of Meningococcus.

Stage of Incubation.

Stage of Invasion.

Stage of Advance : acute stage : temperature, pulse, appearance, nervous system, skin eruptions, termination of acute stage by death, convalescence, or the chronic stage.

Chronic stage : hydrocephalus, temperature, mental condition, nervous symptoms, course and termination.

Complications : Eye complications, deafness, arthritis, &c.

Relapses.

Types : fulminant, ambulant, abortive : Post-basic Meningitis : Meningococcal Septicæmia.

The Blood.

Diagnosis : clinical, bacteriological. The cerebro-spinal fluid.

Prognosis.

Treatment : general management and diet, general treatment, drugs, lumbar puncture, serum treatment, dosage, after-treatment, intravenous injections, type serums, serum sickness, results of serum treatment, vaccines, treatment of convalescence and complications.

Prophylaxis : isolation, quarantine, treatment of carriers, preventive vaccination.

Synonyms—Cerebro-spinal Fever, Malignant Purpuric Fever, Spotted Fever, Post-basic Meningitis. *French*, Méningite cérébro-spinale épidémique. *German*, Epidemische Genickstarre.

ETIOLOGY. Since the first edition of this book appeared, the prevalence of Cerebro-spinal Meningitis in this country and in the armies of the Allies has added much to our knowledge of the subject. Whereas ten years ago it might fairly be said that the disease was almost unknown in Great Britain until the epidemic which affected Glasgow, Edinburgh and Leith, and Belfast in 1907-8, to-day most practitioners have had the opportunity of observing one or two cases, and many, especially those in military hospitals, have seen a comparatively large number. It is probable that small outbreaks will be liable to occur for some years, although demobilization, by removing the conditions which appeared especially to favour the dissemination of the infection, will doubtless lead to a considerable diminution in the total number of cases.

The description of the disease which was given in this chapter originally was based largely on the observation of cases which might almost be said

to have been untreated. Although in 1908 the kindness of Dr. Simon Flexner enabled me to treat 30 cases with his serum, with the result that the fatality rate was halved, the great majority of my patients had not this advantage, and the illness ran what must be regarded as its normal course. Apart altogether from the want of a reliable serum and its intrathecal administration, we had not in those days realized fully the advantage of repeated lumbar puncture as a therapeutic measure, and in consequence the chronic manifestations of the illness were much more in evidence than they have been in our recent experience. As a result the clinical picture of the disease appears on the whole very different from what it did in 1907, and it has to be described as it shows itself when treated with serum and influenced by the judicious employment of lumbar puncture. Nevertheless, to judge from the proportion of fulminant and obviously hopeless cases, cerebro-spinal meningitis, as we have seen it in Edinburgh during the war, has not been of so severe a type as in the 1907 epidemic.

Predisposing factors. There does not appear to be any reason to believe that *climate* is of much importance. Epidemics have been observed in both cold and hot countries, and the disease is to be found in West Africa and the Soudan. On the other hand, *season* often appears to be a determining factor. The great majority of cases occur in the first six months of the year, and February, March, and April show the greatest number of hospital admissions in Edinburgh, although the disease often persists in May and June. It is possible that weather variations are not without influence. Damp cold weather, partly by producing the catarrhal conditions of the nasopharynx suitable for the establishment and activity of carriers, partly by tending to cause windows to be shut and overcrowding to be more probable, would appear to encourage the dissemination of the infection. As regards *age* all agree that young children are more susceptible than adults. In the 1907-9 outbreaks in Edinburgh 73 per cent. of our patients were under 15 years of age, and as many as 47 per cent. were under the age of 5 years. Infants in particular are susceptible, and 14 per cent. of our cases were in the first year of life. The appended table (J), which includes the military and naval cases of the recent epidemic, exaggerates the liability of the age periods of from 15 to 30 years, and the purely civilian outbreak of an earlier date shows a more or less steady decline in susceptibility as age advances. The latter shows also that at all ages fewer females than males were attacked, although the difference is not so marked as in the composite table given in the text. It is clear, then, that *sex* exercises a very definite influence, the difference in incidence below the age of three years being particularly striking.

TABLE J

SHOWING AGE AND SEX INCIDENCE AND MORTALITY

Age period.	Males.			Females.			Total cases.
	Recovered.	Died.	Total.	Recovered.	Died.	Total.	
0-1	2	25	27	4	15	19	46
1-2	4	13	17	3	7	10	27
2-3	6	11	17	7	7	14	31
3-4	4	6	10	5	5	10	20
4-5	4	2	6	4	5	9	15
5-10	8	14	22	8	13	21	43
10-15	7	12	19	8	10	18	37
15-20	24	23	47	3	8	11	58
20-30	36	24	60	7	3	10	70
30-40	8	8	16	2	2	4	20
40-50	4	4	8	2	5	7	15
50-60	1	1	2	0	1	1	3
60-70	0	0	0	0	1	1	1
	108	143	251	53	82	135	386

Showing the sex and age incidence of cerebro-spinal meningitis. The cases comprised occurred partly in the 1907-9, and partly in the 1915-19 outbreaks. The figures include, therefore, cases treated before the intrathecal administration of serum was used and also cases treated with the inefficient serums of 1915. The patients in the first outbreak were all civilian, in the second many were military. The latter group undoubtedly has influenced the sex and age periods between 15 and 40 years.

There seems to be general agreement that *fatigue* must be regarded as a predisposing factor. Severe physical strain, the result of exhausting route marches or of long railway journeys, has preceded the onset of many military cases. The high proportion of newly-joined recruits among the patients in naval and military outbreaks suggests strongly that *change in the conditions of life* must play some part in determining infection. I have been very much struck by the extremely short period of service of the great majority of our military patients, and, in the only definite barrack outbreak which I have witnessed, most of the men affected were recently joined farm servants, who had been called up less than a month before contracting the infection. There is not much evidence that head *injuries* predispose to the disease, but in the 1907 epidemic I collected a fair number of cases with a history of blows or falls on the head. The tendency of parents is to attribute head symptoms to such causes, and in the case of young children it is very easy to obtain the story of some recent fall. Certain illnesses, *influenza* in particular, have been said to increase liability to infection. That any depressing condition would be likely to lower resistance no reasonable person would deny, but it seems improbable that the association of influenza and catarrhal colds with meningitis depends on anything

more than the facilities they give for the active dissemination of germs by the carriers who may suffer from them. In the case of *mumps*, however, another disease which appears occasionally to precede an attack of meningitis, the lymphocytic reaction of the meninges might well predispose them to infection.

The most important predisposing factor in military outbreaks has proved to be *overcrowding*. Cerebro-spinal meningitis has for long been common in barracks. Out of 57 distinct epidemics in France no less than 39 were exclusively barrack outbreaks. It is easy to see how the 'carrier rate' must be increased when men are crowded together with their heads quite close to each other, and, as Glover has shown, there is no more efficient method of limiting infection than the 'spacing out' of beds to a more reasonable distance.

INFECTION AND DISSEMINATION. The infection is derived from the nasopharynx of a carrier or of a patient. As regards the latter, it is singular how seldom one case can be traced to another, and in Edinburgh, in the rare instances of more than one person in the same house being attacked, the patients have usually developed the disease on the same day or at such short intervals after each other that it would appear reasonable to attribute their infection to a common source. No nurse, and no other patient, although for the most part cerebro-spinal meningitis cases have been treated in wards containing also enteric, erysipelas, and pneumonia cases, has ever taken the disease at the City Hospital. In other words, meningitis, when there is sufficient air and floor space and when reasonable care as to cleanliness is exercised, need hardly be regarded as an infectious disease. Healthy **carriers**, on the other hand, have much more opportunity of spreading infection, and, being unsuspected, may disseminate micro-organisms for a long period of time. New carriers are thus brought into existence, and with their multiplication the probability of the occurrence of actual cases of illness is increased. It would appear that susceptibility to the disease is very slight in the vast majority of the population and that but few of those who harbour meningococci actually contract it. What happens, then, is that an epidemic is in reality more one of carriers than of cases, and that, in proportion to the number of the former, the latter may occur merely sporadically, in small outbreaks, or in sufficient numbers to justify the title of an epidemic. It is probable that the average person does not remain a carrier long. It has been said that even the patient himself is usually free from micro-organisms by the fifth day of his illness, and it is doubtful whether many carriers harbour germs for much more than a fortnight. But a minority, who form the class of 'chronic carriers', retain the

meningococci for longer periods, perhaps for from two to three months as an average.

The carrier passes on the germs by the method of spray or *droplet infection* in the acts of coughing, sneezing, or loud talking. Kissing is obviously a still more direct method of infection. The extreme delicacy of the micro-organism and its susceptibility to drying renders it very improbable that *fomites* play any part in its dissemination, but it has been suggested that cups and drinking vessels, imperfectly washed and dried, as at the bars of military canteens, may be a source of danger, and this might well be the case.

The path of infection. The meningococcus, in the first instance, finds a lodgement in the nasopharynx. There has been much discussion as to whether every patient is a carrier or not before contracting the infection. This question has always appeared to me an academic one. That the development of the illness follows the reception of the virus into the nasopharynx very rapidly in some cases admits of no doubt, but we must admit that even in these instances the meningococci must lie in the throat for some time, whether minutes, hours, or days, before penetrating the patient's natural defences. If it only so lies for a few minutes the recipient is surely technically a carrier while it remains there. The point might be debated equally as regards diphtheria, but it does not seem to have aroused any discussion so far as that disease is concerned. On the other hand, it is a remarkable fact that it is a most exceptional occurrence for meningitis to develop in a detected carrier, and we can only conclude that if a person is susceptible at all he becomes infected very shortly after the micro-organisms invade his nasopharynx.

How the meningococcus reaches the spinal canal from the nasopharynx has been the subject of much discussion. The localization of the lesions at the base of the brain has suggested the theory that infection occurs directly along the olfactory filaments by way of the cribriform plate or that the meninges are reached through the sphenoidal sinuses. But if this were so we would naturally expect to find the anterior part of the under surface of the brain markedly affected, which is not often the case. Indeed, in the many autopsies which I have witnessed, the freedom from inflammation of the anterior part of the base has been a very striking feature, a point also emphasized by Maclagan. It is more probable that in the majority of instances the primary lesion is in the cord, to reach which the meningococcus may travel either by the blood or the *lymphatics*. As regards the latter possibility, Stuart Macdonald suggested that the virus was carried to the cervical glands and to the lungs and that it made its way by the perineural

lymphatics to the meninges, as has been stated to be the case in tubercular meningitis. The possibility of the micro-organism being ingested and reaching the lymph stream by way of the bowel and mesenteric glands is regarded as very doubtful. In favour of this theory are the intestinal hyperæmia and the enlargement of the solitary follicles both of the large and small intestine, and also the marked congestion and swelling of the mesenteric glands. Stuart Macdonald, however, has found that these bowel changes occur equally when a primary spinal lesion is made experimentally in the monkey, and it is therefore probable that, as is the case with certain other forms of toxæmia, the intestinal inflammation is merely a manifestation of the disease itself and does not necessarily indicate that the diplococcus is in the first instance ingested. It is now generally held that the virus reaches the meninges through the *blood-stream*, and that, after the formation of the local focus in the nasopharynx, there is a more or less definite stage of septicæmia, the so-called pre-meningitic stage, followed by the localization of the disease in the meninges. The meningococcus has been found in the blood not only in the early stages of the fever but before clinical meningitis is evident, and in certain cases meningitis does not supervene at all. H. D. Rolleston concludes that 'probably cerebral infection through the choroid plexuses (of the lateral ventricles) is the usual though not exclusive site of initial invasion'. Nevertheless, the impressions I have gained from post-mortem examinations and from lumbar punctures suggest that the cord is often attacked first.

MORBID ANATOMY. In fulminant and acute cases the body is usually well nourished. The disease, indeed, seems to attack a high proportion of strong and healthy persons. If, however, the case has been a chronic one, emaciation is usually extreme, the body being literally reduced to skin and bone. Marked deformity may also be present owing to the extraordinary degree of opisthotonos which often occurs during life. Robertson mentions that one of his cases at Leith required a square box for a coffin. If death has occurred early, characteristic hæmorrhages or indefinite petechial spots may be noticed on the skin. Unless the case is of old standing, the surface of the brain is always hyperæmic and sometimes very intensely congested. The typical lesions consist of an acute inflammation of the pia-arachnoid with effusion, sometimes merely turbid, often quite purulent, into the subarachnoid space. In early or comparatively slight cases the upper part of the brain may present congestion only, but usually there is a suggestion of milkiness beneath the arachnoid along the lines of the sulci. Occasionally thick purulent matter plasters the vertex. In the majority of cases, however, the more severe lesions

are concentrated round the base, the under surface of the cerebellum and the pons suffering most. The exudate is gelatinous or purulent in consistence and usually yellow in colour, occasionally with a greenish tint. It seldom extends forward beyond the optic chiasma. The brain itself is œdematous and the ventricles contain purulent fluid, and in cases of long standing may be lined with organized pus. Cases of the fulminant type, which are very early fatal, present occasionally nothing more than very intense congestion of the meninges with some suggestion of milkiness in the sulci. In others, however, in spite of the short duration of the illness, the brain appearances are those of an ordinary acute case. In chronic cases the outstanding feature is a condition of hydrocephalus. The ventricles may be extremely distended, and flattening of the convolutions and thinning of the brain substance as the result of pressure are usually more or less evident. Occasionally gelatinous material is observed in the ventricles and at the base of the brain, but, if the duration of the illness has been much prolonged, the results of the original inflammatory process have usually been absorbed and the surface is pale and shows no congestion.

As regards the cord, the inflammatory changes vary from hyperæmia, which alone may be obvious in very acute cases, to a thick plastering of both surfaces with purulent lymph. The lesions are as a rule best marked on the posterior surface. It is most remarkable how after even three or four days' illness the cord may be found thickly coated with sticky pus, and nothing emphasizes better the difficulties which stand in the way of successful treatment. When the membranes of the cord are opened, a certain amount of turbid or purulent fluid almost invariably escapes. In chronic cases it is not unusual to find the membranes much thickened and firmly adherent in places to the cord.

As regards other post-mortem appearances, Embleton states that Empyema of the sphenoidal sinus is to be found in the great majority of instances. Intestinal hyperæmia is common in early cases, as is enlargement of the intestinal follicles and of the mesenteric glands. Small hæmorrhages are occasionally present in the surface of the heart and lungs. The latter are nearly always congested, and very frequently broncho-pneumonia is present. In fulminant cases hæmorrhages in the substance of the adrenal glands appear to be a constant feature.

BACTERIOLOGY. The diplococcus intracellularis is usually associated with the name of Weichselbaum. It is found in the cerebro-spinal fluid and meninges of persons suffering from the disease, and is said to be invariably present in the nasopharynx in the early days of the illness. It is not uncommonly recovered from the blood; some observers indeed report a very

high percentage of successful cultures at the onset of the fever. It has also been found in the conjunctiva, the fluid of the joints, and the testicle. In appearance it is not unlike the gonococcus. It occurs in pairs and sometimes in tetrads. The inner opposing surfaces of each pair of organisms are somewhat flattened. There is no capsule. When present in the spinal fluid it is often found within the cells of the exudation, although it is not uncommon to find practically all the germs extracellular in a patient who comes under observation early. The meningococcus is a very delicate micro-organism and is easily killed either by heat or cold. Special precautions, indeed, are required if cultures are to be made, and a spinal fluid must be kept warm and cultures placed in a heated box until they reach the laboratory. Frequent subcultivation, also, is required if cultures are to be kept alive. On many media it is difficult to obtain a satisfactory growth, but a medium of agar and ascitic fluid gives good results, and recently trypagar has been largely employed, it being advisable to add a little fresh blood to the slopes at the time the culture is made.

The colonies appear as rounded discs, colourless and translucent, with uniform borders. Young cultures stain well with methylene blue and the ordinary aniline dyes. The diplococcus is negative when examined by Gram's method, but it must be remembered that some strains after subcultivation do not decolorize readily. The differentiation of the micro-organism from other Gram-negative cocci is effected by agglutination and opsonic tests and by a comparison of their power of fermenting different sugars with acid production. For instance, the diplococcus intracellularis ferments glucose and maltose, but leaves lactose, levulose, and various other sugars unaffected. The usual method of identification, however, is by the agglutination test, and if a suspicious diplococcus is not agglutinated by the type serums now obtainable the result is regarded as negative for practical purposes when a search for carriers is undertaken, though we have had a few cases in which cocci were recovered from turbid spinal fluid and failed to agglutinate with any of the four type serums.

Types of Meningococcus. As long ago as the 1907-9 epidemic it was perfectly clear that meningococci, apparently identical in their morphology and cultural characteristics, showed great differences in their agglutinative properties. Houston, and among others Taylor, who was working at the Edinburgh City Hospital at this time, showed that the epidemic strains from Belfast and Edinburgh were apparently identical and were agglutinated indifferently by the blood of patients from either city and also by the serum prepared by Flexner and Jobling. On the other hand, cocci from sporadic cases in London failed to react with the serum of

our patients, and, conversely, our cocci were unaffected by serum from London. In 1909 cocci from several of our patients were not agglutinated by Flexner's serum. I remember discussing some of these facts with Professor Kolle at Sheffield in 1908, and, in view of our recent experience, it is interesting to recollect that he thought very lightly of their practical importance. In 1909 Arkwright distinguished two definite strains of meningococci, one of which he associated with sporadic cases and the other with epidemic, and Dopter also noted agglutinative differences which led him later, in 1911, to use the terms meningococcus and *parameningococcus*. At the present time four types, as distinguished by Gordon, are generally recognized in this country, of which it appears that I and III correspond with the Group A of Nicolle and the meningococcus, and II and IV with Group B and the parameningococcus. That Gordon's types naturally fall into two groups seems undoubted, and, if the type is III, it is usual to find that the micro-organism is agglutinated distinctly, though in lower dilution, by a Type I serum, the same relationship being observed between II and IV (see Table K, p. 584). In Edinburgh we have only typed meningococci since the autumn of 1917, and have found Type I most frequently in our cases, II and III not so commonly, and IV on one occasion only. As will be seen below, the success of serum treatment depends very largely on the serum employed being one which is antagonistic to the particular type of infecting meningococcus.

INCUBATION. In a disease which is much more likely to be contracted from an unrecognized carrier than from an actual patient it is very difficult to estimate the limits of this period with any degree of certainty. But the evidence points to the stage being a very short one, and cases mentioned by Sophian and by Foster and Gaskell lead us to the conclusion that it lasts probably from one to five days, and is usually under four days. We are justified in regarding longer periods with suspicion, for, even if a first case in a house is followed three weeks or a month later by a second, the probability is that some member of the family has remained a carrier and caused the infection.

STATE OF INVASION. The main characteristic of the onset of the disease is its suddenness. There are, as a rule, no symptoms which can be classed as truly prodromal. Some believe in a regular prodromal stage with coryza and post-nasal catarrh. But it must be remembered that most cases of the disease occur when colds are common, that influenzal conditions probably predispose to infection, and that the meningococcus causes some nasopharyngeal catarrh in persons who are merely carriers and who are not in the strict sense 'infected' at all. I have not personally

PLATE XXIX.

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A moderately severe case of Cerebrospinal Meningitis, showing slight head retraction and a profuse crop of herpes.

found coryza a frequent symptom in the histories of my own cases, but even if it existed I should hesitate to regard it as an integral part of the disease. In a few cases slight headache and nausea may last for about twenty-four hours and even pass off altogether before the acute process commences. In others a sharp onset may be followed by a complete disappearance of the severe symptoms for even one or two days, this remission being followed by an attack of ordinary severity. The average patient is struck down from the moment of the first symptom. It is not unusual for a person to go to bed perfectly well and to be found completely unconscious on the following morning. The earliest manifestations of the disease, however, are in most cases vomiting and headache. This initial *vomiting* is almost invariable. I have analysed the early symptoms presented by a series of 152 cases, and find that vomiting on the first day of illness occurred in no less than 119 of those whose history could be accurately obtained, which certainly did not exceed 130. The vomiting is occasionally troublesome, and may persist in the early days of the disease. Unless the patient is completely unconscious, or a very young child, *headache* is always complained of. It is often of an agonizing character and concentrated for the most part in the occipital region. Pain in the back of the neck is also present in most cases, and backache is another common symptom, pain being felt all down the spine and not merely limited to the loins. The *stiffness of the neck* which is such a characteristic feature of the illness is often well marked within a few hours of the onset. The same may be said of head retraction. *Shivering* is also a very frequent symptom at the outset.

In young children the first sign of the disease may be a convulsive seizure, and the fits in some instances are almost continuous till the death of the patient, which under such circumstances is not likely to be delayed for more than two or three days. *Convulsions*, as an initial symptom, were noted in twenty-five, or about 16 per cent., of my cases. All the patients except five were children of two years old and under. One woman of thirty-nine years, however, started her attack with a convulsion. *Delirium* is a not infrequent early symptom, although, as a rule, the patient is conscious enough to concentrate his attention and answer questions for a few minutes at a time. Abdominal pain, sometimes very severe, was complained of in the first twenty-four hours of illness by a sufficient number of patients to lead me to believe that it must be classed as an occasional initial symptom. It may depend on the changes in the intestines and glands which have been noted above. Retention of urine is not infrequently an early symptom.

Lastly, some degree of *fever* is probably invariable at the outset. It may, however, fall very rapidly, as I have seen the temperature normal within twelve hours of the first symptom. Usually, on the other hand, cases which come under observation in the first twenty-four hours of illness have a temperature ranging from 100° to 104° F. (see Figs. 57, 58).

STAGE OF ADVANCE. After a sudden onset of symptoms as above described, there is always a comparatively acute stage more or less prolonged. This may be followed by death, by a reasonably rapid convalescence, or lastly by a long chronic stage which is attended by much wasting and which only too often terminates fatally. It will be well in the first instance to consider the acute stage.

The acute stage. This may last from a few hours to about three weeks, though, if death supervenes, in the great majority of cases it is not before the third day, and, on the other hand, marked improvement and the convalescent stage cannot be expected before the end of the first week. The usual features presented are the following. The patient is flushed and the complexion may show a slight cyanotic tinge. The mind is confused and there is more or less delirium. Adults complain much of headache and pain in the back of the neck, and it will be found difficult to bend the head forward on the chest. The pupils may be unequal, but are usually equal and react sluggishly to light. Strabismus is occasionally present. The tongue is furred and often dry, and the mouth is foul. The temperature is usually, but not invariably, elevated. The pulse varies considerably in rate and character. Insomnia is a common symptom. In the more severe cases petechial spots and moderate-sized hæmorrhages may appear on the skin in the first twenty-four hours. Herpes, especially of the lips, is often noticed. Kernig's sign is nearly always present. The patient is hyperæsthetic and resents touching and handling, and appears particularly sensitive to cold. Lying on his side with the head slightly or markedly retracted he often moans or screams, the pain in the head and back being almost constantly complained of, if he is not asleep. Occasionally there is wild delirium, but as a rule the patient does not attempt to leave his bed. In fatal cases the respiration becomes laboured, though not always rapid, the face is much cyanosed, and purulent discharge pours from the nostrils. The skin becomes dusky and often mottled, and death supervenes, sometimes with hyperpyrexia, occasionally by a relatively sudden collapse. A very large proportion of the total deaths occur in the first week of the illness. In the milder cases the symptoms during the first week remain much the same, though there is some variation in their intensity

in any given patient at different times. On one day the mind may be clear and the headache hardly complained of. The next the patient may be delirious and roaring with the pain in his head and back. This alternation in the severity of the symptoms is often a striking feature of the disease, and compels us to be very careful as regards prognosis.

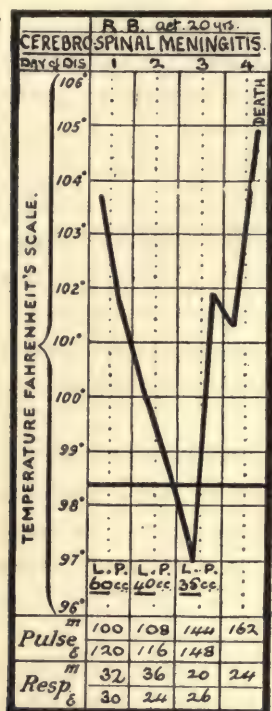


FIG. 57. A severe case, fatal in eighty hours from onset. At the time when the temperature was subnormal was completely unconscious. The letters L.P. indicate the lumbar punctures.

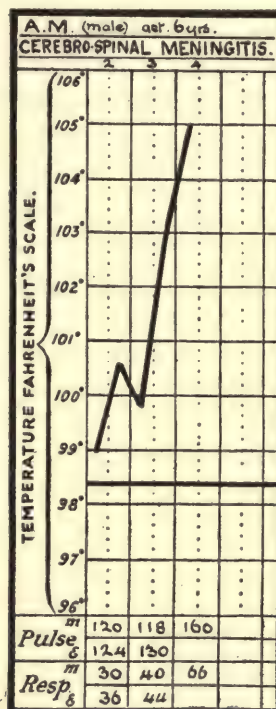


FIG. 58. A very severe case of an almost fulminant type lasting seventy-two hours. Body covered with small hæmorrhages. Unconscious from twelve hours from onset. Hæmorrhages were found post mortem on surface of heart and lungs. Purulent exudate on surface of base of brain and on cord. Vertex congested.

It will now be necessary to consider the above symptoms more in detail, and firstly it will be convenient to consider the course of the temperature. This is extremely irregular. We have seen that there is reason to believe it is usually elevated at first, and we may add that this elevation continues as a rule for the first week of the disease. But it cannot be said to assume any fixed type or to follow any regular curve. This is well shown in the charts which illustrate this chapter. The fever

seems to bear little or no relation to the severity of the symptoms, except indeed at the time of death, when it often reaches a comparatively high level—105° F. or over. But deaths, even in the first week, with the temperature normal or subnormal are not rare. If four-hourly readings are taken, the irregularity of the curve is still more manifest. In some young children there is practically no fever at all, even should the case progress to a fatal termination in the first week. In patients who survive this period the temperature may remain elevated for weeks, or, on the other hand, when the chronic stage is reached it may become normal, remittent, or intermittent.

The *pulse* appears to be as variable a quantity as the temperature. When the patient is restless, and suffering much pain, it is usually small and rapid. During periods of quiescence it is not more raised than would be expected from the height of the temperature, and is often comparatively slow and full. I have not often found it irregular in rhythm or in strength, except indeed when a patient is dying. Before death the rate may be very rapid, usually exceeding 160 if the fatal termination takes place during the acute stage (see Figs. 57, 58).

The *respiration* tends to be rapid and irregular from the first, though some patients show little disturbance. Irregularities of pace and rhythm are perhaps noticed most often when the patient is asleep. In fatal cases it is usual to notice a considerable increase in the number of respirations as death approaches. Biot's breathing, periods of apnoea followed by sighing respiration, is occasionally observed, but is more frequent in the chronic stage, and several of my patients were reported as having died before death had actually occurred. Cheyne Stokes breathing may precede death, but it is unusual to find it during the course of the disease. Sophian associates respiratory irregularity with a greater or less degree of hydrocephalus and considers it as an indication for lumbar puncture.

The *appearance* and attitude of the patient are often characteristic. The face is from the first flushed, and in the more severe cases there is a distinct dusky tinge. The conjunctivæ are sometimes suffused, but as a rule are clear. The patient lies on his side, as this position allows him to keep his head held back. In very severe cases, particularly if the temperature is low, pallor and lividity may early take the place of the flush, and as the sufferer drifts into complete unconsciousness he tends to lie on his back.

The *headache* in many cases is intermittent in character, but in the severer types it is constant and often atrociously painful. One of my patients, a man of over forty, was at times almost maniacal as the result of it, although

he was perfectly conscious and had no delirium. The pain in the neck and back also is often very severe, and even strong men quite break down under the torture which it gives them, and cry like small children. It has been suggested that the head is held voluntarily retracted to mitigate the pain in the muscles of the neck, but this can hardly be the case. The *neck is definitely rigid*, and when an attempt is made to force forward the head there is a strong spasm of the muscles which prevents the forward movement, the head sometimes jerking further back as the result of the attempt to straighten it. In young children, even in the early acute stage, there may be also arching of the back, but marked opisthotonos is not to

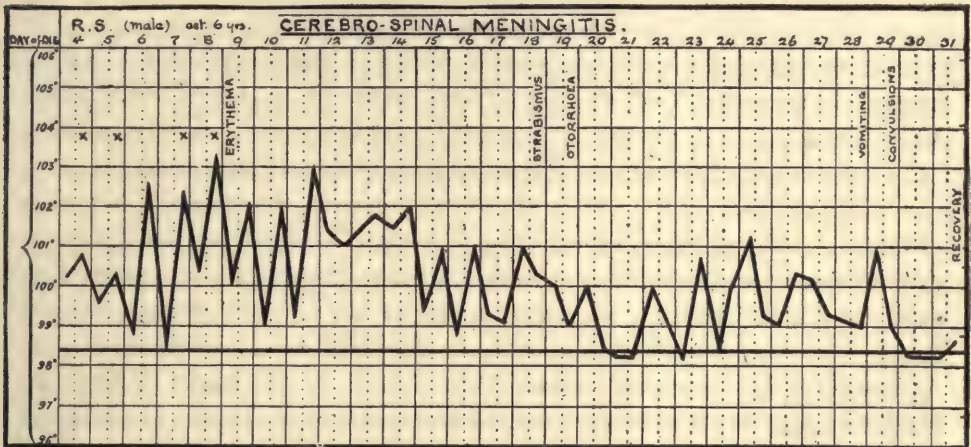


FIG. 59. Illustrating the irregular course of the fever in a patient who ultimately recovered. From the thirty-first day till the ninety-fourth, when patient was discharged from hospital, the temperature remained steadily normal. He suffered from convulsions, emaciation, and facial paralysis during his long convalescence, and vomited at frequent intervals.

be expected till the chronic stage. *Head retraction* is not invariable, but rigidity of the neck muscles is always present unless the patient is profoundly unconscious, when Kernig's sign is often found wanting also.

As regards the *mental condition*, it varies markedly from time to time. One of the most interesting features of the disease is the mental clearness of many patients almost to the last. It is sometimes almost impossible to believe, when one is present at an autopsy and sees cord and base covered with thick pus, that only the day before the patient was talking intelligently. This condition of the mind is an argument in favour of the primary lesion being a spinal one. It must be admitted, however, that the average patient suffers from some mental confusion, and only enjoys complete

consciousness at intervals, if at all. *Delirium*, indeed, is usually present in a greater or less degree, though in many patients only at night. Occasionally it assumes a maniacal character, but even then the pain which the patient suffers usually keeps him in bed, and I have not had the same trouble in controlling patients of this type as is the case with typhus or small-pox. Towards the end of a fatal case coma often supervenes, and we have already seen that complete unconsciousness may be present in some patients during the whole brief course of their illness.

A fairly constant condition is what is known as *Kernig's sign*, which is also present in other forms of meningitis. In health, when the thigh is flexed at a right angle on the abdomen, it should be quite easy to extend the leg on the thigh. In attempting to do this, however, in a meningitic patient, complete extension is prevented by a spasm of the hamstring muscles which forces back the leg as it is gradually raised. I have found this sign present in 92 per cent. of a series of 216 cases, the observation being made on admission. In a number equalling 5 per cent. of the whole, however, it is recorded as 'slight', and it might, perhaps, be more accurate to say that it was absolutely definite in 87 per cent. The patients who failed to show it were for the most part either deeply unconscious or moribund. This may explain the fact that in the much more severe outbreak of 1907 the sign was only positive in 70 per cent. Many of those who failed to give it were infants, a somewhat remarkable finding, as the sign is said to be unreliable in children of under two years of age because their legs are often rigid and normal infants may give a positive result. For this reason some have preferred *Brudzinski's sign*. When the neck is flexed the patient flexes the legs by raising the knees, and on passive flexion of the leg on one side the opposite leg is either flexed with it or definitely extended, the so-called contralateral reflex. The latter I gave up after a short trial, but the neck sign appears usually to be present and seems reliable. It must of course be understood that both these signs merely indicate the presence of some form of meningitis. The *reflexes* are very variable. The knee-jerks are occasionally abolished, but are quite often present. The plantar reflex is frequently absent. An interesting point is that the abdominal reflex is usually absent from the first. Out of forty-eight cases, in which on admission the abdominal muscles were not held by excitable or delirious patients too firmly for accurate observation, I only found this reflex present in nine. This seems to point to the lower part of the cord being early implicated by the inflammation, as has been pointed out by Fowler.

Another common symptom is *hyperæsthesia*. The patient often objects to light and may try to keep his head constantly covered. He is apt

to be irritable when touched, and there is sometimes great tenderness down the line of the spine. But the most pronounced feature is unquestionably the extraordinary sensitiveness to cold manifested by a high proportion of patients. They seldom seem to find the ordinary allowance of bedclothes sufficient. When an attempt is made to uncover a child for purposes of examination the determination and rapidity with which he hauls up the bedclothes again is almost comic. Needless to say, these remarks do not apply to patients who have sunk into a condition of coma.

In a small minority of cases the *convulsions* which may have ushered in the disease continue during the whole acute stage, which, as might be expected in the circumstances, is very early terminated by the death of the patient. Twitching of the face and limbs may also occur during this period, though it is rather in the chronic stage that they are to be expected.

Strabismus, often transient in its nature, is not uncommonly present in the acute stage. The squint appears to be of a spasmodic character, is often divergent, and varies much in amount from day to day. The pupil reflex is usually present, but often a little sluggish. Inequality of the pupils is sometimes noted even in the first days of the illness. Discharge from the eyes, due to a slight degree of conjunctivitis, must be classed among the early symptoms. It is of importance in that it probably depends on a meningococcal infection, and the disposal of the discharges therefore demands care. But many patients, the vast majority indeed, do not suffer from conjunctival inflammation at all. Hæmorrhages have been seen on the conjunctiva in rare instances, occasionally in association with a hæmorrhagic eruption elsewhere, sometimes alone. Optic neuritis is not a common early symptom, but is said to occur in a certain number of the cases. Nystagmus in the acute stage is rare. It may be noted that the examination of the eyes is often rendered extremely difficult by a tendency to spasm of the lids, which are apt to close tightly when touched. This appears to be an involuntary movement and not due to photophobia. Ptosis occurred in 3 per cent. of our cases, all of which terminated fatally.

A certain degree of *rhinitis* may be present from the onset. Occasionally a large amount of foul purulent discharge pours from the nostrils, and I have noticed this most frequently in very acute cases shortly before death. Some congestion of the fauces is often observed, but actual sore throat is hardly ever complained of. That, however, a comparatively acute inflammatory process often occurs in the naso-pharynx there can be little doubt. The *tongue* often gives but little indication of the severity of the case.

Should the fever be prolonged for a few days it may become very foul and heavily furred, and sordes frequently collects on the lips and teeth. *Vomiting* occasionally persists from the commencement of the illness, but it is more usually seen in the chronic than in the acute stage. When it does occur it depends on nervous rather than on gastric causes, and is unaccompanied by nausea. The appetite is often, indeed usually, astonishingly good, and there is little difficulty in persuading the patients to take an adequate amount of nourishment. Constipation is the rule in the early days of the fever and most cases require enemata or aperients.

Cutaneous eruptions are frequently seen, although the somewhat unfortunate popular name for the disease, 'spotted fever', has perhaps given them an undue prominence. The most important of them is the *hæmorrhagic*. This is met with in two forms: firstly, the petechial, in which small spots like faded flea-bites, not exceeding in size the head of a pin, are scattered more or less profusely over the surface of the body; and, secondly, the purpuric, which consists of larger hæmorrhages into the skin. These purpuric spots are usually irregular in outline, and, when fresh, are maroon in colour, becoming later of a dull purple hue. In size they vary from the head of a pin to a quarter of an inch in diameter. They may be seen in any part of the body, but, if not very numerous, are to be looked for chiefly on the lower part of the trunk and the inside of the thighs. Occasionally they have been noted as present on the eyelids and even the conjunctiva. It is almost needless to add, they are not raised above the skin and do not disappear on pressure. These hæmorrhagic eruptions are not nearly so common as the term 'spotted fever' would imply. They were present in 22 per cent. of my 1907-8 cases, but in only 14 per cent. of the 216 cases of the more recent epidemic. Billings in his analysis of 2,180 cases states that they occurred in 19 per cent. They are an early manifestation of the disease. In one of my patients a well-marked purpuric eruption was visible within twelve hours of the first symptom, and in many the spots were well marked on the second day of illness and had doubtless occurred earlier. They are observed in meningococcal infection without meningitis and are undoubtedly a manifestation of the septicæmic stage of the disease.

Another form of eruption, the *herpetic*, is relatively common and often of great value in diagnosis. It usually assumes the form of herpes labialis (see Plate XXIX), but it may occur in almost any part of the body, and I have seen it on the cheeks, the hands, the elbows, the trunk, the nape of the neck, and the lower extremities. One of my patients showed it on the tongue. It was present in 21 per cent. of my cases in 1907 and in 26 per cent. of the recent group, but in some epidemics it is not so common, and Billings reported



Hemorrhages of varying sizes on the skin of a Meningitis Patient.

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it in only 11 per cent. of the New York cases. It is a relatively early symptom, appearing most frequently on the third and fourth days and in the great majority of cases during the first week. Its first appearance, however, may be postponed till later and it may show itself for the first time or reappear should the patient have a relapse. Herpes is rarely seen in very young children, but I have observed it in a baby of six months and in two other children of under two years of age. After the age of five it becomes a very frequent symptom, and it occurred in 45 per cent. of the children between five and ten years in the recent epidemic. Thereafter, all age-periods showed a high percentage incidence, the figure being as much as 36 per cent. for patients above 30 years, and 34 per cent. for those between 10 and 30 years. Perhaps the ages between seventeen and twenty-five would present an even greater proportion. It may be remarked that the meningococcus can sometimes be recovered from the herpetic vesicles.

Lastly, erythematous eruptions are also liable to occur at the onset or during the course of the disease. They occurred in one-sixth of a series of sixty-six patients who were not treated with serum. Since the introduction of serum treatment it is impossible to distinguish any which may occur in the course of the disease from serum rashes, but they were present at the moment of admission in 7 per cent. of my cases. They are usually ill-developed roseolar or blotchy rashes and are not likely to be mistaken for any of the exanthemata. They are best marked on the extremities and disappear quickly, but occasionally leave behind some staining which may become petechial. Sometimes, indeed, the arrangement of a petechial eruption suggests that it has been determined by the earlier presence of some rash of this type. Other rashes are definitely papular and appear to affect the neighbourhood of the joints. Erythema was occasionally observed at all stages in the untreated disease, and the rashes were observed in patients of all ages.

A livid erythema accompanied by vesicles filled with blood has been described by Osler as occurring on the extremities. The vesicles dry up, leaving papular nodules which may persist for some days. One of my cases developed an eruption approximating to this type. A papular erythema appeared on the elbows and knees. The patient at the time had been ill fifteen days and was vomiting almost constantly. She was much cyanosed and the limbs were of a dull purple colour and spotted with many small petechial hæmorrhages. Definite hæmorrhages also occurred into the raised papules, which were grouped and arranged much in the manner of a herpetic eruption. The papules became distinctly nodular and were palpable for over a fortnight. The patient ultimately went home well.

Some enlargement of the *spleen*, especially in the more acute cases, is occasionally observed.

The *urine* is in most cases normal, except in so far that it assumes the usual febrile characteristics. Some degree of albuminuria, usually slight, may be present in a small number of cases. True nephritis occurred in only two of my patients. The urine does not give the diazo reaction even in the acute period. Both retention and incontinence of urine are comparatively common in the early stages, particularly, of course, in comatose patients.

The condition of the *spinal fluid* will be described under the head of 'diagnosis'.

TERMINATION OF THE ACUTE STAGE. Death is the most common termination. It occurs in a very large proportion of cases within a week of the onset, but it may be postponed, even when the symptoms remain acute, for two or three weeks. The end is sometimes sudden, the condition of the patient changing for the worse with little or no warning, the pulse, for instance, remaining reasonably good and the respiration easy till from five minutes to an hour before death. The patient collapses, and in a few seconds is pulseless. He may rally for a little, if appropriate treatment is employed, but the improvement is only slight and does not as a rule last long. Only one of my patients survived a collapse of this type, and he ultimately recovered. In this mode of death the temperature falls rather than rises. The termination, however, most frequently met with is for the patient to fall into a condition of coma, with laboured breathing and marked cyanosis. The pulse becomes rapid and not infrequently uncountable. The temperature runs up and may attain hyperpyretic levels, and death rapidly supervenes. Even in cases of this type the change for the worse may be quite unexpected. The temperature and pulse in the morning may both be normal. Twelve hours later the thermometer may register 107° or more, and the pulse be impossible to count (see Fig. 62).

Convalescence. Fortunately, however, all patients do not succumb to the disease. About the end of the first week the symptoms may abate, seldom very abruptly. In certain cases treated with serum the improvement may be so marked as to fairly deserve the name 'crisis'. But the ordinary rule is that, even if the temperature falls rapidly, the rigidity and headache persist for a few days, and there is a tendency to temporary exacerbation of the symptoms at intervals. Rigidity of the neck is usually long in disappearing, and Kernig's sign may persist even longer. Till these have disappeared we cannot feel at all satisfied with the condition of the patient. The convalescents take their food extremely well, and, once the

symptoms have completely subsided, progress rapidly. The sooner this change for the better occurs the less chance there is for the case running a chronic course. But in not a few instances the acute stage lasts three weeks before any definite improvement is noted, and even under these conditions the patient may make an uneventful recovery, untroubled by any of the nervous phenomena which mark the chronic stage. In favourable cases the duration of the patient's stay in hospital is sometimes as short as three or four weeks.

The chronic stage. On the other hand, when the more acute symptoms subside, the patient may enter on a stage which is far removed from convalescence. It is difficult, indeed impossible, to define the exact moment when the acute stage runs into the chronic. Perhaps as good an indication of the latter as any is the advent of well-marked *wasting*. We have seen that, in spite of their headache, their delirium, and other troubles, the patients during the acute stage take and digest their food admirably. There is not, then, much ordinary febrile wasting to be observed during that period. But later on, however well they take nourishment, and many take it in truly amazing quantities, a definite progressive emaciation manifests itself which must be regarded as one of the outstanding features of the illness. The loss of flesh is literally appalling. It is not associated with fever metabolism, as it is quite as well marked in patients with normal as with subacute temperatures. It must depend on some trophic changes connected with the profound disorganization of the nervous system. The patient progressively wastes until he is reduced literally to skin and bone. It must be recollected, however, that the emaciation may be extreme, and yet recovery not absolutely impossible.

It is practically certain that the symptoms usually associated with the chronic stage depend upon the existence of **hydrocephalus**. Serum treatment, by its effective action on the meningococcus and its toxins, does much to prevent the blockage of the foramina which may interfere with efficient drainage of the ventricles, and the drainage itself by means of lumbar puncture at suitable intervals gives time for the re-establishment of normal conditions in the central nervous system and prevents further damage being done by the continued intracranial pressure. As a result, the chronic stage has been seldom observed in our cases in the recent epidemic, the exceptions being chiefly infants who often come under treatment late, sometimes even with hydrocephalic symptoms fully developed. The most obvious symptoms of chronic hydrocephalus are irregular pyrexia, intense headache, causeless vomiting, mental feebleness, paralysis of the cranial nerves, and muscular rigidity. Children frequently give the purposeless 'hydrocephalic cry'.

In infants bulging of the fontanelle is a marked feature, and Macewen's sign, a resonant note on percussion over the lateral ventricles, can often be elicited after the sutures have closed. In adults it is difficult to be certain of this sign. The description, given below, of the symptoms and course of the chronic stage is based on my experience of the disease before the introduction of serum treatment and systematic lumbar puncture.

The *temperature* is extremely irregular. It may be quite normal, or even subnormal, and remain steadily so for weeks. Often, again, it is remittent,

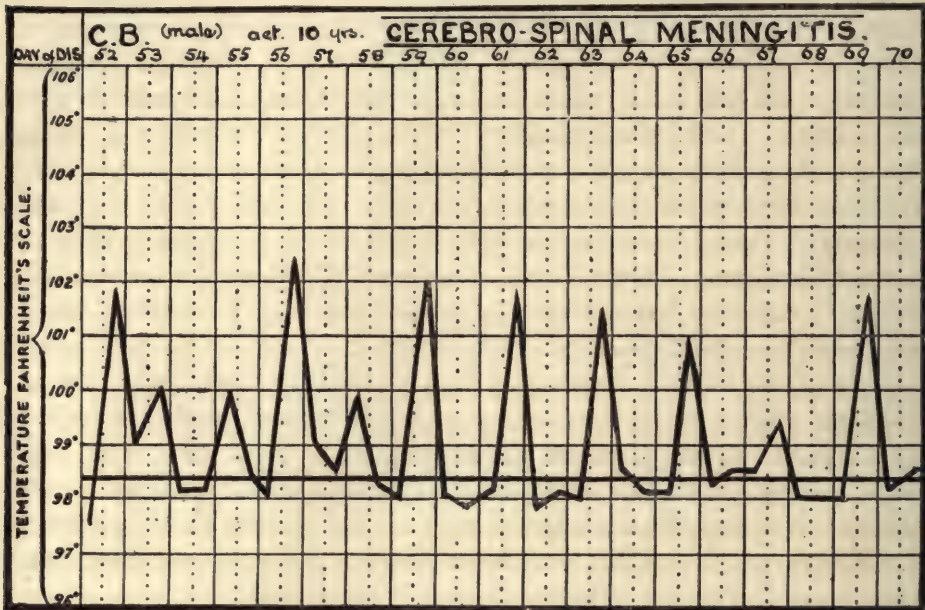


FIG. 60. Showing intermittent temperature in a chronic case from fifty-second to seventieth day.

the morning readings being somewhat in the neighbourhood of the normal line, while at night levels of anything from 100° to 103° may be reached. Sometimes, though more rarely, it may present true intermittence, as is well shown in the chart (Fig. 60), and in such cases the symptoms may show exacerbation with each increase of the fever. Lastly, the temperature may run an irregular subacute course, varying very much in height from day to day and showing well-marked remissions at unexpected times.

During the chronic stage the *mental condition* of the patient may vary considerably. In some cases, except for occasional delirium at night, the mind may remain clear almost to the end. In others some mental weakness is manifest. Many adults become quite childish, though, should recovery

ensue, the mind usually returns to the normal as the patient regains strength. In some patients, particularly children, the mind seems to become temporarily blank and no interest is shown in anything except food. Obviously the deafness and blindness which are not infrequently present may have something to do in dulling the intelligence, but this apathy is often seen in patients who have the full use of their special senses. Occasionally severe attacks of headache cause restlessness and noisiness and sometimes even wild delirium. The patient, just as in the acute stage, varies much from day to day, both as regards his intelligence and the severity of his symptoms.

The main features of the disease, neck rigidity, with more or less head retraction, and Kernig's sign persist through the chronic stage. When they pass off it may be taken as a probable sign of convalescence. In young children especially the *head retraction* becomes very marked and *opisthotonos* is often present in a greater or less degree (Plate XXXI). The occiput may sometimes be almost in contact with the buttocks. The legs may be drawn up, but they are not infrequently completely extended and quite rigid. *Rigidity* of the limbs, indeed, either temporary or persistent, is frequently observed in the chronic stage.

Of other *nervous symptoms* we may in the first place mention the apparently causeless vomiting. Some patients vomit almost every day. Others may have freedom from this symptom for one or two weeks, and then vomit at frequent intervals for several days. Others, again, do not suffer from vomiting at all. The appetite is quite unaffected. The patient will throw up a whole meal and then be perfectly ready to start again with another one. Another frequent symptom is twitching of the face or limbs. Occasionally there is tremor, which in some patients is almost constant. Others suffer from rhythmical spasms of different muscles, various movements following each other in a cycle which is frequently repeated. Actual convulsions may terminate the case, or may last for several hours with ultimate recovery. Such convulsions occurred in 20 per cent. of my patients who survived the first week, and in the majority of these they were first noted in the late chronic stage.

Among other features may be mentioned *ptosis*, and paralysis or spasm of the ocular muscles with resulting *strabismus*. These manifestations may be only transient, which suggests that they depend more on irritation than actual structural changes of the nerves. Occasionally, however, they persist to the end. *Nystagmus* is comparatively common in the more severe cases, and constant winking movements of the lids may also be seen. A sign often associated with hydrocephalus is retraction of the lids.

This gives an appearance of undue prominence to the eye. Conjugate deviation of the eyes may be observed, particularly in unilateral convulsions, but sometimes quite independently. Conjugate rolling of the eyes has also been noted. Facial paralysis occurred in at least three of my cases.

Involuntary passage of both urine and fæces is common. This increases the tendency to bed-sores, for which the extreme emaciation and low trophic condition of the patient are responsible. Another interesting feature, connected no doubt with trophic changes, is the occasional formation of blisters on various regions of the skin. These blisters closely resemble those caused by the careless use of a hot-water bottle, and when I first saw them I was inclined to blame the nursing. But it soon became obvious that they occurred in patients in whose bed no hot bottle had been used, and they appeared, moreover, in situations which rendered it impossible that they could have been caused by pressure. Unless carefully attended to, they were very apt to degenerate into sloughing sores. No patient who developed them recovered.

Course and termination of the chronic stage. A patient, then, earlier or later in his illness, but usually within three weeks of the onset, commences to show progressive emaciation. This, accompanied by some or all of the symptoms detailed above, may go on increasing. The patient gradually loses strength, and in many cases, although marked relaxation of all the worst symptoms may be occasionally noted for days at a time, drifts into a state which may be most aptly described as one of vegetation rather than of life. Apathetic and often apparently unconscious, sometimes blind, frequently stone deaf, he lies absolutely motionless unless some convulsive seizure puts his wasted muscles into temporary action. Occasionally headache or pain in the back is sufficiently severe to make him cry out; sometimes, indeed, he literally roars for several minutes at a time. Continuing to waste till the bones seem to project through the skin, and till the most efficient nursing fails to prevent the almost inevitable bed-sore, taking greedily the food that is offered him, but showing no other interest in life, or in some cases even requiring to be fed through a nasal tube, he at last succumbs, perhaps two or three weeks after death has seemed imminent. Such cases sometimes present the risus sardonicus several weeks before the end. As to the mode of death, it may come, as it were, imperceptibly, or in a convulsion.

On the other hand, a patient may remain in the chronic stage for some weeks and the symptoms may gradually pass off, the last to disappear being usually Kernig's sign. A curious result of the long-continued head retraction is the frequency of temporary paresis of the muscles of the neck.

When the patient tries to sit up the head falls forward on the chest and wobbles helplessly from side to side if the trunk is moved. I have observed this paresis also in a few children whose illness never became chronic. The convalescent is left very feeble and it is usually several weeks before he can use his legs with any freedom. Mentally he is often weak and childish until he has regained his full strength. Too often he carries with him the permanent disability of total deafness. Headache, sometimes of a severe character, may recur at intervals for some months. The convalescence of the chronic, as of the acute, case is liable to be interrupted by recrudescences.

As regards the *duration of illness*, several of my chronic cases were over three months in hospital, one patient, who recovered, going out after 105 days. One death occurred as late as the 146th day. Several other fatal cases ran a course of eighty days or more. It may be assumed that, once chronic symptoms have appeared, progress either to death or recovery will be extremely slow, in marked contrast, in fact, to the rapid amelioration so frequently shown by patients who pass directly from the acute to the convalescent stage.

Complications. It is not very easy to make a distinction between the more unusual symptoms of the disease and its actual complications. Of the latter, *broncho-pneumonia* occurs comparatively frequently and is occasionally of importance in determining a fatal result. Lobar pneumonia has been present in only a few of our cases. Bronchitis has not been common, but in one patient, in whom it was present on admission, it was largely responsible for the fatal result. Nephritis, as we have seen, is rare. It has been observed both in the acute and chronic stages, however, and two of my patients, out of a total of 386, presented it. Both pericarditis and endocarditis may occur, but do not appear to be very common. The heart murmurs which were occasionally found present in my own series did not appear to be due to actual endocarditis. I have not seen a case of phlebitis.

It is obvious that certain *nervous complications* depending on lesions to the central nervous system and its membranes are likely to occur. Facial paralysis is occasionally observed, and was noted twice in my 216 recent cases. Hemiplegia only occurred in one of the same series; Rolleston has reported it as present in 12 out of his 502 naval cases. MacLagan had three cases of paraplegia in his 400 patients. In one it was due to a cerebral hæmorrhage, in the other two, which recovered, it was apparently caused by the pressure of inflammatory products. Monoplegias have been described.

Meningeal infections other than meningococcal are occasionally noted as complications or sequelæ of cerebrospinal meningitis. Septic mixed infections have been reported as due to lumbar puncture or to otitis. Tubercular

infection is very rarely associated with the disease, but may occasionally occur, and one such case appears in our records. In another influenza bacilli were found together with the meningococcus. Pneumococcal meningitis is more common, and Netter and Salanier reported 22 cases of secondary pneumococcal infection. I have had the misfortune to lose two patients from this cause. Both had apparently recovered after treatment with Flexner's serum and the fluid was clear and sterile. In each case meningitis reappeared and death followed rapidly, in one patient in 14 hours, and pneumococci were the only micro-organisms present. Infection of this sort has been attributed to a special vulnerability of the meninges after injections of serum.

Eye complications. Besides the paralytic or irritative manifestations already mentioned, such as strabismus, ptosis, and nystagmus, which are more common in the chronic stage than in the acute, and have therefore not been so frequently noted in my recent cases, other eye conditions fall to be considered. The occurrence of sero-purulent inflammation of the conjunctiva is frequent enough in the early stages of the disease to be regarded rather as a symptom than a complication, particularly as some of these cases undoubtedly depend on the meningococcus. Even in the chronic stage the eyes may continue to discharge. Ulcer of the cornea occurred in two or three of my cases, and in one instance this was followed by perforation of the anterior chamber and ultimately the collapse of the whole eye. Of our recent 216 patients only three developed *iridochoroiditis*, which appeared early, in the first week of the illness, some prominence of the eyeball and the collection of greenish pus in the anterior chamber being the most obvious features. Two of these patients died, the third recovered with loss of the sight of the affected eye. Optic neuritis is not uncommon in the chronic stage, and its frequency in the acute stage has been differently estimated, some observers reporting it in 65 per cent. of their cases. *Blindness*, either temporary or permanent, may be observed at all stages. Eleven of our 386 patients died at a sufficiently advanced period of the disease to make it certain that this sequela existed, but the sight of all the patients who recovered was perfectly normal when they left hospital. The blindness, like the deafness, depends on central rather than on local lesions.

Deafness. In 1907 I found otitis media a not uncommon complication among children, especially in the chronic stage. Recently it has been very unusual. The deafness which in former times so frequently followed meningitis is due to central causes and is a nerve deafness. In the pre-serum days 16 of our patients who survived the first fortnight of the illness were totally deaf, and those who ultimately recovered are recognized as incurable. Serum

treatment has diminished the percentage incidence of this complication, which was only noted in nine of our last 216 cases, three of the patients not surviving, while in half the remainder the deafness was partial or limited to one side. In most of these cases the condition was present on admission; the complication, indeed, has not uncommonly fully developed by the second day of illness.

Arthritis. The frequency of this complication has been variously stated, and I have had difficulty in distinguishing it from the joint inflammation associated with the serum disease, as in diphtheria it is not very uncommon to find arthritis without any trace of rash. MacLagan reports it in from 10 to 15

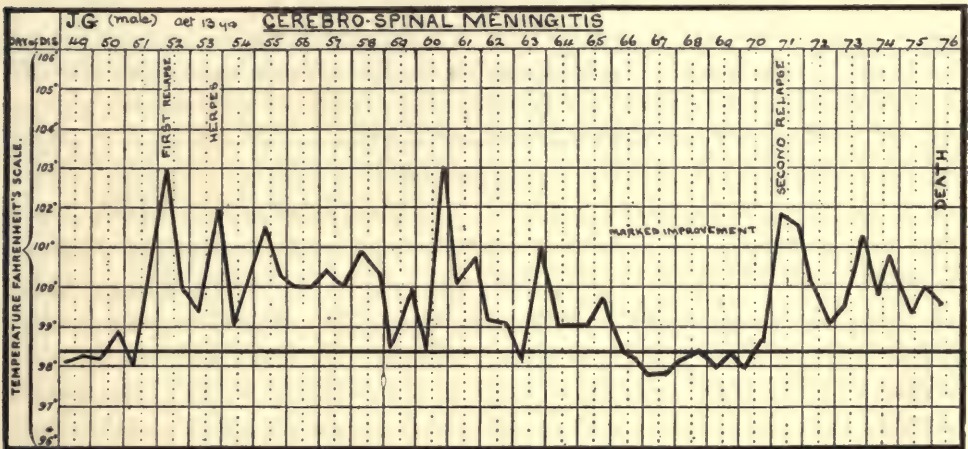


FIG. 61. Illustrating relapses. Patient admitted eighth day of illness. Continued fever till thirty-first day. Thereafter improved, and except for persistence of Kernig's sign was apparently well. On fifty-first day relapsed and was once more desperately ill. Fever gradually declined and, although much emaciated, patient improved rapidly from sixty-fifth to seventieth days. On seventy-first day again relapsed and died on seventy-sixth day. Treated both in original attack and relapses with Flexner's serum, of which he received in all 360 c.c. by spinal injections.

per cent. of all cases, and puts the most likely time for its occurrence about the fifth or sixth day. I only felt certain of it in three of our 216 recent cases, and it was not much more common in the pre-serum group. It is due to blood infection, and the meningococcus may be sometimes but not invariably recovered from the fluid, which may be clear, slightly turbid, or definitely purulent. The larger joints, knee and elbow, seem to be most frequently affected, and the lesion is a synovitis. The condition is usually short lived. *Orchitis*, and epididymitis, caused in the same way, are occasionally observed. It was recognized in only two of our 216 cases, but slight degrees of inflammation may have been missed. A fair average incidence appears to be from 3 to 4 per cent.

RELAPSES. The definition of a relapse, always difficult, is particularly so in this disease, and, as I have been widely quoted as having an unusually high percentage of them in comparison with the experience of others, it may be well to devote a few lines to this question. The general opinion seems to be that recrudescences are common and that relapses are comparatively rare, although Netter speaks of the comparative frequency of '*rechutes*', the same word that is employed for a typhoid relapse. I am quite prepared to admit that some of the conditions which I named relapses in 1907 were possibly due to hydrocephalus. In the days before serum treatment we were not so ready to lumbar puncture, and the condition of the fluid between the attacks was not always noted. But I think the analogy of enteric fever is quite a good one, and no one hesitates to class as a relapse any repetition of that fever which occurs after a definite apyrexial interval without symptoms, however short that interval may be. In that fever a *recrudescence* is what has been also termed an intercurrent relapse, an exacerbation of the fever, with increasing pyrexia and a return of classical symptoms, interrupting the lysis. I have been accustomed, then, to class as a relapse in meningitis a return of the classical symptoms after an apyrexial interval during which the fluid has been clear and sterile, and I would be inclined to reserve the name of recrudescence for a case in which the symptoms had largely disappeared while micro-organisms could still be cultivated from the fluid. I grant freely that one cannot expect the disappearance of Kernig's sign, which usually remains so long with the meningitis patient, but the same may be said of enlargement of the spleen in enteric fever, which, it is well known, persists during the apyrexial interval in patients who relapse. Judging by this standard I had 7 cases of true relapse in 53 patients treated with Flexner's serum in 1908-9, at a time when the state of the fluid in the interval was always considered, that is to say in over 13 per cent. In the recent epidemic, however, I have only had 2 true relapses in 216 cases, and I believe that in meningitis, as in enteric fever, the proportion of relapses varies very much in different outbreaks. On the other hand, lumbar puncture for pressure has been performed much more freely of late years, and it is possible that by preventing slight degrees of hydrocephalus it renders the patient less susceptible to reinfection and also encourages the drainage of the recesses in which the meningococcus is probably harboured until it once more invades the whole sub-arachnoid space. This seems a more likely explanation of the cause of relapses than that of reinfection from the nasopharynx, and it may be mentioned that Maclagan failed to recover meningococci from that situation in some of his relapsing patients.

All the initial symptoms which we have noted as accompanying the onset

of the primary attack are liable to be present. A patient apparently quite convalescent may be struck down at once and die within thirty-six hours. I recollect one woman who, in the middle of eating a substantial dinner, suddenly became unconscious and had symptoms pointing so distinctly to a cerebral hæmorrhage, including hemiplegia and conjugate deviation, that I was not convinced of the real nature of the case till I attended the autopsy. Other patients who went to sleep apparently well were found unconscious or in convulsions during the night. The temperature rises, headache, retraction, and other characteristic features are once more prominent, and herpes may appear for a second time. As a rule the febrile condition lasts for only a few days, but there is a great risk of a case which relapses becoming chronic. More than one relapse in the same patient is not very rare and I had under my care a man who had six distinct attacks between June 23rd and Dec. 31st, during which time he was twice discharged from hospital as perfectly cured. *Second attacks* after longer intervals have also been reported.

TYPES. It is by no means easy to classify with any accuracy the different forms assumed by the disease. There are, however, in addition to the type described above, which, as we have seen, may vary much in severity, two fairly well-marked varieties, the fulminant and the mild. The **fulminant** type includes those cases which run to a fatal termination in anything from a few hours to about three days from the onset. The most striking features are either wild delirium or profound coma, more usually the latter, marked cyanosis, and many definite purpuric spots. The temperature may not be high, and, indeed, shows that variability which is so characteristic of the disease. Death sometimes occurs very early. My own shortest case was twelve hours from start to finish, but cases have been reported of death within five hours of the onset. Three patients in my series died within twenty-four hours. The **mild** type of the fever may be taken to include the so-called *ambulant* and abortive cases. It is beyond all question that the whole course of the disease is represented in some instances by a passing attack of severe headache and pain in the back of the neck. This is accompanied by moderate or slight pyrexia. The true nature of such attacks would not even be suspected were it not for their appearance in connexion with cases of the ordinary or fulminant types or perhaps for the presence of labial herpes. The duration is extremely short and the symptoms so mild as to hardly justify even the slight risks of lumbar puncture. In *abortive* cases the attack may be of average severity, but the illness is suddenly cut short in a few days, and the patient has a rapid convalescence. There is little real

distinction between these varieties. We have seen that in the ordinary form of the disease convalescence may commence about the end of the first week, and it is difficult to say before which particular day of the disease a return to the normal is to be held as an abortion.

We occasionally meet with cases in which, although active treatment with serum is carried out, the fluid becomes scantier and more purulent at each puncture until perhaps it ultimately refuses to flow at all. The name of '*suppurative*' has been given to this class, but it is doubtful if it is a really definite type. An ordinary pneumococcal meningitis usually shows this peculiarity, which in cerebro-spinal meningitis may well depend upon the use of a serum not suited to the case and a poor natural resistance to the infection on the part of the individual.

Post-basis Meningitis in infants is defined by H. D. Rolleston as chronic encysted meningococcal meningitis in young infants, and we may agree with him that its special features appear to depend on the early age of the patients. Many of the cases appear to start much more insidiously than does the usual form of the disease, but the type is rapidly assumed by many infants who present the sudden onset and classical symptoms of the more epidemic form. The course of the illness is usually chronic, eruptions are unusual though not unknown, blindness is comparatively common although deafness is said to be rare, and well-marked hydrocephalus is a frequent sequel. Great distortion and exaggerated opisthotonos are prominent features, and rigidity of the limbs is often noticed. The child is apt to lie with the forearms pronated and the thumbs turned into the palm. A certain number of patients recover, but they carry with them the traces of the disease in the form of imbecility, blindness, or hydrocephalus.

Meningococcal Septicæmia. In certain cases meningococci infect the blood and do not reach the meninges. Doubtless in a certain proportion of them an excessive dose of the virus or a special susceptibility on the part of the patient is the cause of a fatal termination before meningitis has had time to develop, and there is little to distinguish such an illness from the fulminant form of almost any acute infection, the main features being prostration and extensive hæmorrhages into the skin, and especially, it is said, the adrenal bodies. On the other hand, cases have been reported of comparatively mild attacks of fever due to the presence of the meningococcus in the blood, and in others a septicæmia has been observed to exist for months with intermittent or irregular pyrexia, erythematous rashes, herpes, orchitis, and joint affections. Such a fever may also follow an ordinary attack of meningitis. It is obvious that there is great difficulty in diagnosing such cases. Only one meningococcal septicæmia without meningitis occurred in my series and was of

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Cases of Cerebrospinal Meningitis in the chronic stage, showing opisthotonos and emaciation.

the fulminant type. In two cases the micro-organisms were found in the blood before meningitis developed. Both were admitted on their first day of illness.

THE BLOOD. Some degree of leucocytosis is probably present in all cases, the count being seldom less than 10,000 during the acute stage, while it may rise to nearly 50,000. The increase in leucocytes is due to an increase in the number of polymorphs. The count rises with each exacerbation, but in the few cases in which I have been able to follow it I have not found it of any value for prognostic purposes. The highest number of leucocytes noted was 45,000, of which 94 per cent. were polymorph cells.

DIAGNOSIS. The accurate determination of the diagnosis is a bacteriological question and can only be made after lumbar puncture. For practical purposes, then, the main problem is in what circumstances should lumbar puncture be performed? In determining this it is well to remember that, whereas irreparable harm may result from delay, there is very little risk attached to the operation itself, and that, when there is a reasonable presumption that meningitis may possibly be present, it is unquestionably our duty to perform it.

First among the **indications for lumbar puncture** I should put neck rigidity. This is probably the most constant sign in cerebro-spinal meningitis and was recognizable on admission in over 95 per cent. of the cases. Any patient presenting it, or the signs of Kernig or Brudzinski, should certainly be punctured. Sudden unconsciousness, in a child or young person particularly, may be an example of the so-called apoplectiform onset of the disease, and, in the presence of an outbreak or epidemic, it is certainly wise to puncture. Hæmorrhagic eruptions associated with headache and vomiting also form an indication for puncture, and in cases with head symptoms, but otherwise doubtful, the presence of herpes has more than once persuaded me that it would be wise to examine the spinal fluid. When the disease is prevalent it is folly to postpone puncture because the indications for it are not absolutely clear. At other times there might be some justification in awaiting such definite calls for puncture as neck rigidity or Kernig's sign. The procedure of lumbar puncture is described on a subsequent page (p. 575).

Clinical Diagnosis. The presence of *neck rigidity* is usually sufficiently obvious. It is best appreciated when an attempt is made to flex the head on the chest. Many patients also object to lateral movement. It will be found occasionally that flexion of the head is performed fairly easily when first attempted. If this is the case it is wise to repeat the movement several times, a procedure which may result in a very definite spasm of the neck

muscles being set up. It must be remembered that deeply comatose and moribund patients may have little or no rigidity and that both the neck sign and Kernig's sign may be absent. Patients as ill as this, however, are always worth puncturing. Another difficulty may be that the patient may first come under observation at a time when there is a definite remission of his characteristic symptoms. In many cases this remission occurs about the second day of illness and signs which were quite definite during the sudden onset of the day before may be entirely absent or elicited only with difficulty. This *period of remission* has been particularly emphasized by Netter and by Foster and Gaskell, and my own experience of it has been very similar. I therefore puncture on very little in the way of definite indications, if the case strikes me as suspicious and is from 24 to 60 hours ill.

As regards *head retraction*, it is often not very well marked in the early days of the fever, although the head is usually held straighter than is customary in an ordinary patient in bed. On the other hand, when it is present it is always a valuable sign. It must be remembered, however, that many normal children lie with the head somewhat retracted.

The comparative frequency of *retention* of urine in the male adult at the onset of the disease led Foster and Gaskell to put great stress on this complication as an aid to diagnosis. It certainly occurs much more frequently than in most of the acute fevers, and its presence, when taken together with severe headache and sudden onset, must, I think also, be regarded as suspicious. The condition of the *reflexes* has never helped me in diagnosing the disease. The knee-jerks are most variable. The abdominal reflex appears to be absent in the great majority of cases, and to that extent may be worth investigating.

The mental condition of the patient is often quite clear for long periods, even in severe cases. The practitioner is warned not to be misled by this peculiarity. A patient will sometimes discuss his symptoms quite rationally and a few hours later may be found unconscious.

Differential Diagnosis. The diseases most likely to be confused with cerebro-spinal fever are firstly the various forms of meningitis and secondly those acute infective conditions during the course of which head symptoms may develop. As regards the former group, we must first consider tubercular meningitis, which accounted for 28 out of 192 cases which were notified as cerebro-spinal fever or as 'observation' for that disease. In making a distinction we are largely influenced by the history of the case. The onset of *tubercular meningitis* is much more insidious, and the disease may start with moderate headache accompanied by vomiting at intervals, often continued for two or three weeks before grave head symptoms are obvious,

only four of 21 recent cases reaching hospital in the first week of their illness. While rigidity and retraction may both be present, they are seldom so obvious nor are they nearly as constant as in the meningococcal variety, and the lateral movement of the head is usually good. Herpes is extremely rare, and no instance of it occurred in this series. On the other hand, strabismus and ptosis are more common and the abdomen is much more likely to be scaphoid, a condition only found in prolonged wasting cases of cerebro-spinal fever. A very slow, or extremely irregular, pulse is more characteristic of the tubercular infection. The appearance of hæmorrhages on the skin on the one hand, or the detection of tubercles in the choroid on the other, would determine the question. But the symptoms of both diseases demand lumbar puncture, and the character of the fluid is usually decisive. A tubercular fluid is clear, or almost clear; the cells contained in it are lymphocytes. Glucose, in my experience, is usually present, though often in comparatively small quantities, the amount varying much in the course of the disease. Dubois and Neal report finding bacilli in 65 per cent. of tubercular fluids examined, a much better result than we have attained in Edinburgh, though, they state, inferior to the percentage of successes secured by Hemingway. In making the distinction it must be remembered that in some meningococcal cases the fluid clears up rapidly and lymphocytes increase in numbers, and that therefore, if the patient comes late under observation, the examination of the fluid may not be absolutely final.

Of other forms of meningitis the most common is *pneumococcal meningitis*, which occurred 25 times in the group of wrongly diagnosed cases. Here bacteriological diagnosis is the only method of distinction. The clinical symptoms are exactly the same, herpes not infrequent and even purpuric rashes occasionally present. This condition may follow a pneumonia, in which case the presumption is in favour of a pneumococcal origin, but in the cases which have come to the City Hospital, though pneumonia was occasionally present, it did not precede the meningitis. No doubt, when it does so, the patient usually finds his way to a general hospital and the cause of the meningitis is correctly diagnosed. The fluid in the pneumococcal case is extremely purulent and is apt to decrease in amount and to become more sticky. It often has a greenish tinge, but I have observed this also in meningococcal cases. Glucose is invariably absent.

Of the other *septic varieties of meningitis* much the same may be said. My list includes two due to streptococci, one to staphylococci, and one of uncertain bacteriology, probably Friedländer's pneumo-bacillus. The septic cases, and occasionally the pneumococcal ones, are often associated with some local focus of infection, such as a discharging ear or a septic wound,

the presence of which may be of assistance in diagnosis. Meningitis may also be influenzal, and one such case occurs in this series.

I have not had an instance of syphilitic meningitis in this group of cases. The condition might well be mistaken for the tubercular infection. The fluid is clear and contains lymphocytes. The symptoms generally appear to be subacute. When epidemic poliomyelitis is prevalent its meningeal form may be mistaken for cerebro-spinal meningitis, and Netter considers that its differentiation may be exceedingly difficult. Here again, however, the fluid is clear and 90 per cent. of the cells are lymphocytes. If paralysis is present the diagnosis is rendered more easy, as it is relatively uncommon in cerebro-spinal fever.

On the whole there is less difficulty in differentiating cerebro-spinal fever from other acute infections complicated with meningeal symptoms. It must be remembered that the toxins of various diseases, notably those of typhoid and pneumonia, are capable of setting up a condition of meningeal irritation which closely simulates a true meningitis. Such symptoms as head retraction, a meningeal cry, strabismus, twitching and the like may all occur in the course of an acute disease and yet be followed by complete recovery. Again, it is usual, should such a case come to the post-mortem table, to find no obvious changes in the meninges to account for these head symptoms. This condition has been named by Dupré '*meningism*', a convenient term for describing a group of symptoms depending on toxæmia. It may appear early in an acute infectious disease; indeed the comparative suddenness of its onset has been said to distinguish it from a tubercular meningitis. It is, therefore, all the more likely to be mistaken for cerebro-spinal fever, a disease of typically abrupt onset with early head symptoms. In my own list of wrongly diagnosed cases thirty-five seem to have been sent into hospital on the strength of meningeal symptoms occurring comparatively early in the course of an acute disease. Nineteen of these had lobar pneumonia, and in few were physical signs very obvious on admission, three typhoid, eight broncho-pneumonia, and one each typhus, diphtheria, and scarlet fever. It is interesting that in none of these patients was Kernig's sign definitely present, a point which is quite in accordance with the descriptions of meningism by Tylecote and others, and also with my own experience of the condition in typhoid, scarlatina, and diphtheria. It may be noted that influenza is excluded from these figures.

A case of *lobar pneumonia* with flushed and slightly cyanosed face, somewhat retracted head, and well-marked headache and delirium, and perhaps also with herpes appearing on the lips may, if cerebro-spinal fever is epidemic, be very difficult to distinguish from the more severe com-

plaint. The rapid breathing, however, will probably arouse suspicion, and it is possible that some definite signs may be found in the lungs. Should a whole lobe be found to be affected the probabilities are all in favour of the case being one of pneumonia alone. The lesions complicating cerebro-spinal infection are more likely to be broncho-pneumonic, though it is well to remember that cases of pneumonia affecting a whole lobe have been reported as due to the diplococcus meningitidis. Should the examination of the chest be negative, it is wiser not to wait for physical signs to declare themselves but to perform lumbar puncture at once, and I believe that the puncture may be of considerable therapeutic value. To assist us in the diagnosis of enteric fever we have Widal's test, and also the diazo reaction, which in the cases of cerebro-spinal fever examined for it, and it was looked for in many, was always absent. Also, if the idea of the possibility of enteric occurs to us, we may find confirmatory evidence in the examination of the patient himself. *Typhus* is a much more difficult distinction if the case is seen late enough for the eruption to have become petechial, but the rarity of this disease makes the question somewhat academic. The eruption in typhus, except in the very rare fulminant form, comes out slowly and passes through stages before it is definitely hæmorrhagic. The purpuric spots and petechiæ of cerebro-spinal fever may appear in the first twenty-four hours of the disease, and delirium and coma are much earlier symptoms. The irregularity of the meningitic temperature as contrasted with that of typhus is also very marked. And, lastly, the diazo reaction has been present in all cases of typhus in the acute stage in which I have looked for it. Another disease which may closely simulate the milder forms of cerebro-spinal meningitis is *influenza*. Apart from the fact that it is occasionally associated with meningism, the sudden onset, violent headache, and pain in the back, and sometimes at the back of the neck, may give a strong suggestion of the more serious disease. During the war 44 cases of influenza were admitted to our cerebro-spinal wards, a few of whom only had any real meningeal symptoms. Even when pain in the neck is complained of, genuine spasmodic rigidity cannot be detected, and not many of the patients required puncture. Their number is no doubt accounted for by the fact that in many instances a true case of cerebro-spinal fever had recently occurred in their barracks or ship.

In most of the conditions mentioned above the chances are that the acute symptoms will be much relieved by the subtraction of fluid and the subsequent relief of pressure. The relief, indeed, is both more marked and more permanent than in cases of meningitis, and of itself justifies the procedure. But obviously the main value of the puncture is diagnostic. Lastly,

the possibility of a true meningitis complicating any of the diseases named must be remembered.

Of other conditions affecting the brain which may occasionally cause confusion, we may notice cerebral tumour, three cases of which are included in my series. The history and symptoms of the case should as a rule prevent any mistake, but when an epidemic is present it is easy to see how any obscure head symptoms may cause cerebro-spinal fever to be suspected. Thus three cases of cerebral hæmorrhage and one of thrombosis figure in our records. A case of heat-stroke was also admitted.

I have had five cases of encephalitis lethargica, all of which it was considered advisable to lumbar puncture. The fluid is clear, and cells, chiefly lymphocytes, are few. The appearance of these patients is not particularly like that of a meningitis, and their lethargy is in marked contrast to the irritability so often met with. Ocular paralyses are more common.

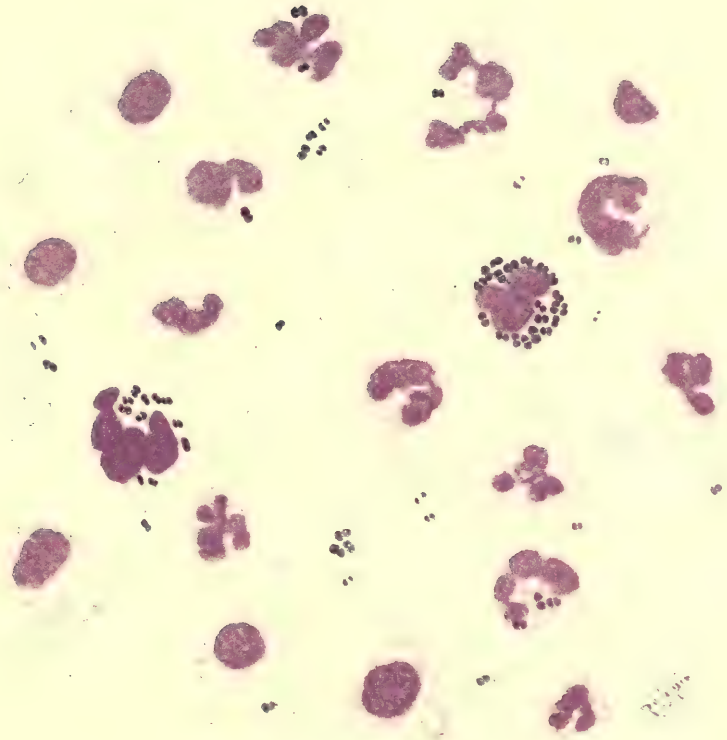
Other mistakes in diagnosis which have come under my notice often appear to depend on a want of appreciation of what the characteristic symptoms of cerebro-spinal fever are really like. Thus in four patients rheumatism, lumbago, and sciatica were sufficient to give the impression of neck rigidity or Kernig's sign. A rubella case was sent in on the strength of a complaint of headache and stiff neck, and, more remarkable still, the stiff neck and erythematous rash of a genuine case caused its notification as rubella. A patient with purpura and definite meningitis was sent in as malignant measles.

An interesting case, also reported by H. D. Rolleston, was one of osteomyelitis of the spine with pus in the extradural space, which, flowing fairly freely on lumbar puncture, seemed to confirm an impression that the patient, who had had severe pain in the back, was suffering from meningitis.

A few patients suffered from nothing more than hysteria. If this is suspected, lumbar puncture without an anæsthetic usually puts an end to the symptoms and at the same time excludes meningitis.

Bacteriological Diagnosis and the Cerebro-Spinal Fluid. The simplest method is the direct examination of the cerebro-spinal fluid, which is obtained by lumbar puncture as described below (p. 575). Its appearance alone is of considerable importance. It is, in cases of cerebro-spinal fever, turbid to a greater or less degree during the whole acute stage. In bad cases, even within a few hours of the onset, it may be actually purulent and of a greenish yellow colour, a sticky deposit of pus being thrown down in the test-tube on standing. In the mildest cases the fluid may be merely cloudy, and the deposit very slight. In the chronic stage there may be no turbidity present, though even then any cells found present in the

PLATE XXXII.



Pus from lumbar puncture from case of Cerebrospinal Meningitis.
Meningococcus in the pus cells, and also free. Degenerated forms are also
present.

Leishman's stain. $\times 1000$ diameter.

fluid will be polymorphs, in contrast to the lymphocytes found in the clear fluid of a tubercular case. It must be recollected that in pneumococcal and septic meningitis the fluid is turbid or purulent, and cannot be distinguished either by its appearance or microscopically from that of cerebro-spinal fever, except by the recognition of the micro-organisms present in either case.

A *smear preparation* of the fluid will, if suitably stained with methylene blue, show, in addition to polymorph cells, a varying number of diplococci, some of which are almost certain to be intracellular even in the early days of the disease. Many, however, will be lying free. Later on, as the fluid clears up, the intracellular forms will be found to predominate. The diplococcus is Gram negative, that is, it does not retain the stain when treated by Gram's method. The coloured drawing (Plate XXXII) shows a highly magnified smear preparation stained with Leishman. It will be noted how some cells seem to pick up many more micro-organisms than others. I find it convenient to incubate a tube of the fluid, and occasionally meningococci may be found when a direct smear shows none. Cultures from the fluid may be made on tryptagar, but it is wisest to leave the cultural tests in the hands of a competent bacteriologist. The same applies to any effort made to isolate the diplococcus from the conjunctival or nasal discharges, or from the fluid in blisters or herpetic vesicles. The agglutination test with type serums has simplified the identification of the meningococcus, and it is wise to determine the type in any case, especially if therapeutic type serums are available.

The fluid at first contains little or no glucose, which is also absent in septic cases, but is always present in a non-meningitic patient, and appears irregularly in a tubercular fluid. The presence of albumin and, in particular, globulin, denotes the existence of meningitis. I have no experience of the globulin test (Noguchi's) which is said to be very reliable, but I believe valuable indications can be obtained, especially in prognosis, from the routine employment of Fehling's test for glucose.

Occasionally the fluid presents a yellow colour, usually as the result of some slight hæmorrhage, often at a former puncture. More rarely it coagulates immediately in the test-tube, forming a jelly-like mass, the 'syndrome of Froin'. This is often associated with adhesions and is said to be a fatal sign, but one of my patients presented it and ultimately recovered.

The question has been raised if it is justifiable to call a case cerebro-spinal meningitis if meningococci cannot be found. In my own opinion it may be quite legitimate to do so. Given a turbid fluid, polymorphs,

signs of meningitis, and such a symptom as herpes, for example, it is difficult to see what else the condition can be, especially if it is followed by recovery. The septic cases do not recover, and the micro-organisms which cause them are much less likely to be missed in the fluid than is the very delicate meningococcus.

Prognosis. The mortality of the disease is naturally a high one, and in the days before serum was introduced was estimated at from 20 to 80 per cent. But it is very doubtful if bacteriologically proved cases, when untreated, would ever show a general death-rate for all ages of less than 50 per cent. and for the general population in England during the war the case-fatality rate was about 64 per cent., although many of the patients must have received serum treatment.

The first consideration in prognosis is undoubtedly whether a reliable serum is available. If the patient has this advantage the chances in favour of his recovery are about two to one. If not, it is very doubtful if even judiciously repeated lumbar puncture can give him more than an even chance, if the question of age is left out of consideration. The results of serum treatment are discussed on a subsequent page (p. 586).

Age influences prognosis very considerably. The table on a preceding page (p. 534) shows that of 46 infants of under one year only six recovered, and that the mortality is also very high in the second year of life. After that age the deaths are not so numerous in proportion, and perhaps the period between 10 and 30 years gives the best results. A definite increase in fatality after that age is usually reported, but there is not much difference shown in the table.

Broadly speaking, the more abrupt and severe the onset the more dangerous the case. Persistent vomiting, repeated convulsions, and the early appearance of coma are usually fatal signs. A profuse crop of purpuric spots within the first thirty-six hours points to an extremely severe case. As regards the height of the pyrexia we cannot expect to obtain much assistance in prognosis from the study of the chart. But I am inclined to believe that when the general condition is obviously very grave the patient whose temperature is low or normal has less chance of recovery than one with high fever. The possibility of the temperature being normal shortly before death is illustrated in the charts (Figs. 57, 62). On the other hand, a fall of temperature, together with an amelioration of the other manifestations of the disease, is of excellent augury. It has been already hinted that the condition and rate of the pulse affords us but little assistance. It often remains relatively satisfactory to within a few hours of death. More reliable as a guide is the respiration rate. If this becomes rapid,

whether from pulmonary congestion or an actual broncho-pneumonia, the outlook is very bad.

The early appearance of hæmorrhages, as has been noted, is a grave sign. A certain number of patients who have presented merely petechial spots will recover, but recovery when a purpuric rash has appeared is most rare. No less than forty-seven out of sixty-two patients presenting one or other of these hæmorrhagic eruptions died. Without necessarily suggesting that herpes is a favourable sign, it may be remarked that the death-rate of the Edinburgh cases with this eruption was lower than that for the whole outbreak. On the other hand, many patients die before the symptom is likely to develop, and it would be unsafe therefore to lay much stress on such statistics. In any case herpes is not a bad sign.

The mental condition of the patients is often deceptive. Even if the mind remains always clear a cautious prognosis must still be given. A patient will sometimes talk quite sensibly, and yet twenty-four hours afterwards he may be dead and the autopsy may reveal a brain covered with exudation up to the vertex. On the contrary, delirium of the maniacal variety or the appearance of coma leaves little or no hope of survival. It may be added that, as in the other acute diseases, alcoholism greatly prejudices the chances of recovery.

When the acute symptoms have subsided and the temperature is normal the outlook is reasonably good, provided that rigidity of the neck muscles and Kernig's sign have disappeared. But should these symptoms persist, and should there be any sign of progressive emaciation, it may be concluded that the patient has to run all the risks attendant on the chronic stage. Even if there is no emaciation, the persistence of a definite Kernig's sign should always suggest the possibility of a relapse.

In the chronic stage the most hopeless symptoms are repeated convulsions, tremor, twitchings of the muscles, and nystagmus. Only three out of twenty-one of my patients who suffered from convulsions in this stage

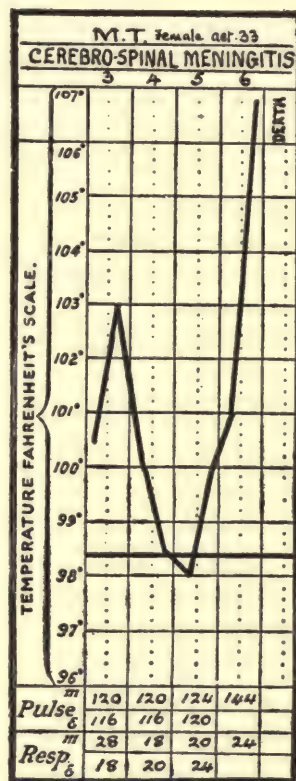


FIG. 62. A very acute case, showing the irregular course of the pyrexia and how little it can be relied upon for prognosis.

recovered, and the mortality of those who presented the other symptoms mentioned was even more formidable. The blisters which have been alluded to as sometimes occurring in prolonged cases are always a fatal sign. Should the emaciation be so extreme that it is impossible, on pinching the skin, to feel any subcutaneous tissue, there is no hope of recovery. But it is truly remarkable how far the wasting can go without a fatal result. Ptosis, nystagmus, and hemiplegia are all extremely bad signs.

The study of the spinal fluid may be of some assistance in the early days of the disease. A large number of extra-cellular diplococci suggests a sharp case. If they gradually become intra-cellular it may be assumed that the patient is improving. Fragmentation, swelling, alteration of staining properties, or loss of viability on the part of the micro-organisms are, judging from cases treated with serum, signs of improvement. As regards the appearances of the fluid itself, it may be said that the more purulent the fluid the less is the chance of recovery. If in the acute stage the fluid is only slightly cloudy, the outlook, if suitable treatment is available, is decidedly hopeful. Too much disappointment should not be felt if it is a little more turbid the day after the first injection, an event I have often noticed and which may be due to the introduction of the serum. But if the fluid continues to become more purulent and its amount decreases, the outlook is very serious. A gradual reduction in the percentage of polymorph cells with an increase of lymphocytes is usually a good sign.

As long as micro-organisms can be recovered from the fluid we must regard the patient as seriously ill. Even when the fluid is quite clear, if there are any symptoms of the chronic stage or if emaciation is present, there is still grave risk.

As regards remote prognosis, the sequelæ of the disease, as apart from the nerve deafness which is permanent and which has often become obvious before treatment has commenced, depend very largely, as Foster and Gaskell have pointed out, upon increased intracranial pressure. They should not, therefore, be numerous in patients who have been carefully watched and lumbar-punctured when necessary. I have had no case of marked mental change or imbecility in our recovered patients, with many of whom we have been in touch for over ten years.

TREATMENT. When in the post-mortem room we see a thick purulent exudate covering both the brain and cord of a patient who has, perhaps, only survived the onset of his attack for three or four days, it is only natural that our feeling regarding the curative treatment of the disease should be one akin to absolute hopelessness. An infection which can cause such extensive lesions in so short a time would appear to be quite beyond the

reach of ordinary therapeutic measures. Yet, since the introduction of serum treatment, we have reason to hope that, provided the patient comes under observation sufficiently early, even the presence of thick pus in the spinal canal does not entirely take away all hope of an ultimate recovery.

General Management. It is in the first place highly desirable that all cases should, if possible, be treated in hospital. The risk of infection, although in reality so slight as to demand little consideration except in the case of soldiers in crowded barracks and dwellers in congested tenements, none the less makes an excellent excuse for enforcing *isolation*. Not only does the hospital patient have the advantage of being attended by doctors and staff familiar with the technique of lumbar puncture and serum administration, but the latter is rendered much more satisfactory when its results can be promptly checked by a laboratory on the spot. Distance from hospital need not be seriously considered, as the cerebro-spinal fever patient tolerates transportation wonderfully well and several of our cases were brought in by ambulance from places more than twenty miles away.

As in other acute diseases, good *nursing* is very important. The necessity for great care of the skin in an illness in which wasting is often such a prominent feature, and in which the trophic functions of the nervous system are so evidently profoundly disturbed, scarcely needs to be emphasized. The patient requires frequent change of position and frequent tepid sponging, and the back should be rubbed with alcohol twice daily. The toilet of the mouth, including the swabbing of the fauces and the whole cavity with some mild antiseptic ointment, should be made at frequent intervals according to the gravity of the case, and it has been suggested that attention to this detail may, by rendering less septic the original site of infection, exercise a certain influence on the actual progress of the patient. The eyes, which in some outbreaks are not uncommonly inflamed, should be regularly bathed. The occurrence of any change in the respiration, or the sudden supervention, especially in early convalescence, of severe headache, giddiness, or vomiting, should be at once reported.

Before discussing the use of serum, it will be well to consider the diet and general treatment of the patients. During the acute febrile stage the **diet** should at first be entirely fluid, consisting chiefly of milk and beef-tea and similar preparations. If the digestion is good, as is usually the case, there is no need to wait for the temperature to become normal before adding semi-solids, such as milk puddings, oat-flour porridge, jellies, and the like. Having in view the marked tendency to emaciation so characteristic of cerebro-spinal fever, it would, indeed, appear that liberal feeding is especially indicated, and that the patient's strength should be, so far as possible,

supported to resist the wasting when it supervenes. Once the temperature is normal solid food can be given freely. The appetite of the patient is often voracious, and, as long as there is no sign of diarrhœa, which is occasionally troublesome in the chronic stage, there is no reason why he should not satisfy it. Vomiting, depending as it does on purely nervous causes, need not be regarded as a contra-indication.

Occasionally it may be found necessary to resort to the use of the nasal tube for patients in whom opisthotonos may be so extreme as to cause a mechanical difficulty in swallowing. For the most part, however, even when there is much retraction of the head, the patients swallow sufficiently well. Nasal feeding may also be required in some cases of coma.

As regards **general treatment** it consists chiefly of treating symptoms as they become troublesome. A not infrequent condition at the outset of the fever is *retention of urine*. The bladder should be most carefully watched for this, and it is a good plan to use the catheter early and frequently, say thrice in the twenty-four hours, as, if undue distention is prevented, control is much more readily re-established. The distressing *headache* is often much relieved, if only for a few hours, by the lumbar punctures necessitated by the serum treatment, especially if, even after the injections, the total relief of pressure has been considerable. Such drugs as phenacetin and caffeine are occasionally successful, and cold applications to the head or the employment of the ice-cap are well spoken of by some authorities. Most patients in the acute stage suffer from *insomnia*, and, if this is accompanied by delirium and excitement, it is often very difficult to relieve. Simple cases often do best with chloral and bromide, either given in hypnotic doses at night or administered in more moderate amounts every four hours. Restless and sleepless children in particular are much benefited by bromidia given in 15 or 30 minim doses throughout the day. For adults veronal is occasionally effective as a hypnotic, but I have obtained better results with sulphonal (gr. 25 in hot toddy given in the late afternoon and supplemented with a drachm or two of paraldehyde or a moderate dose of bromide 5 or 6 hours later). Excited and maniacal patients require morphia, or morphia with hyoscin, hypodermically, and one or two injections are usually well tolerated, but it is wise, if possible, to avoid giving more. For pains in the back and limbs nothing is so effective as the *hot bath*, the patient often obtaining so much comfort that he falls into a natural sleep. When the bath is not possible, hot fomentations may be applied to the back. The restlessness and delirium of children is also much improved by bathing, and, as they are easy to handle, I use baths largely in their treatment, often giving four or five in the twenty-four hours.

Systematic Treatment by Drugs. Few will desire to make use of such remedies if a reliable serum is available, but experience has taught us that circumstances may compel us to supplement our treatment in any way we can, should the serums at our disposal prove ineffective. Perhaps *urotropine* has been most largely used, as it is alleged to reach the cerebro-spinal fluid and might therefore be supposed to exert some antiseptic action. Foster and Gaskell, however, after a sufficient trial concluded it was inert, and personally I never had any reason to believe that its systematic administration was of any value. There is, perhaps, more to be said in favour of *soamin*, H. D. Rolleston having collected 27 naval cases treated with this remedy with a fatality rate of 33 per cent. The method of administration is by intramuscular injection, and doses of 3 to 5 grains may be given to adults, the injections being made daily for the first two or three days and repeated thereafter at longer intervals if required. The drug is not very safe, as optic atrophy has been reported as following its use, but in the series of cases mentioned no such accident happened, although one patient received a total dose of no less than 40 grains. My own experience of *soamin* is very limited, but on the whole I should be tempted to use it, in conjunction with systematic lumbar puncture, if at any time serum were unprocurable.

Flexner has satisfactorily proved by experimental methods that such substances as *lysol* and *protargol*, injected into the spinal canal, are unlikely to be effective, as they not only tend to prevent the emigration of leucocytes into the spinal fluid, but actually diminish the phagocytic activity of the leucocytes themselves. It is improbable, moreover, that the action of these drugs upon the tissues can be harmless. Again, while they certainly damage the meningococci, they do not succeed in destroying them.

Lumbar Puncture as a form of Treatment. There is no doubt that systematic drainage of the intrathecal space by repeated lumbar punctures is of great therapeutic value. It relieves intracranial pressure and its results, lessening the chance of the case becoming chronic, and increases the possibilities of the natural cure of the disease. The removal, moreover, of large quantities of infective micro-organisms can only be to the advantage of the patient. Foster and Gaskell, whose observations were made at a time when no reliable serum was procurable in Great Britain, concluded that the success of serum treatment depended upon the free drainage which is so often entailed by its use. They had a mortality rate of 30 per cent., which shows what can be effected by simple lumbar puncture and would be more impressive if their patients had not been all soldiers and of military age. With a reliable serum I have had a death-rate of 15 per cent. for a similar number of military and naval cases at a time when our total mortality,

including that of infants, was considerably higher than theirs. Indeed the age of the patients and the day of illness when they came under treatment must always be considered in comparing statistical results, and in my experience service patients come under treatment much earlier than do civilians. None the less, lumbar puncture is itself an extremely valuable therapeutic agent. By preventing hydrocephalus, or at least lessening its incidence, it must diminish the occurrence of sequelæ, and, when injecting serum, I always endeavour at the same time to reduce pressure.

Laminectomy and continuous drainage have been practised in a few cases, but the results to be expected can hardly justify such a treatment, especially as it is obvious that the method, like lumbar puncture itself, would be certain to fail when the symptoms depend on encysted collections of fluid in the ventricles.

Serum Treatment. In the 1907 epidemic I made use of a number of serums, including those of Jochmann, Kolle, and Ruppell, without obtaining any satisfactory results. At that time subcutaneous administration was the rule, and serum given by that route does not appear to have much chance of reaching the spinal canal. We owe to Flexner the introduction of the intrathecal method which has been so successful in reducing the mortality of the disease, if the serum employed is suitable to the case. The serum prepared by Flexner and Jobling in 1907 proved itself efficient as regards the type of infection prevalent in Belfast and Edinburgh at that time, and the case fatality in both cities was reduced by more than one-half from the moment of its introduction. A little later Dopter was able to claim equal success for the serum prepared by him in Paris.

As is the case with other serums, the horse is the animal used to supply the antitoxin. The method of immunization is first to inject gradually increasing doses of a vaccine, cultures of the meningococcus being exposed to 60° C. for thirty minutes. For the vaccine live cultures in increasing doses are afterwards substituted, the injections being made every seven days. Alternately with the cultures injections of an autolysate, prepared from the diplococcus, are given. The injections are subcutaneous, but a more rapid method of immunization by intravenous administration has latterly been introduced.

The serum thus produced appears to have a distinctly bactericidal power. Its action is to disintegrate diplococci which are exposed to its influence. There is reason to believe that it also has some antitoxic power. Some of the type serums prepared recently by the Medical Research Committee are definitely stated to contain an antitoxin to the endotoxin of the disease, and difficulties in obtaining results in cases infected by Type II seem to

depend on failure to produce a suitable anti-endotoxin for that variety of the meningococcus.

Unfortunately, when the disease appeared in England in 1914 it became apparent that the particular types of meningococcus which were chiefly responsible for the outbreak had not been employed in the preparation of the serums which were at that time available, and as a result serum treatment must be admitted to have been a miserable failure. By 1916, however, the difficulty had been met and several very reliable polyvalent serums, prepared by the immunization of horses against a very large number of different strains of the meningococcus, had become available. I have had most experience of those of Flexner and of the Lister Institute, but have no doubt that others as effective can be obtained. The work of Gordon and the recognition of the types described by him led to the preparation of serums appropriate to each variety, and for the last year I have followed the method of starting injections with a polyvalent serum and, after the case has been typed, continuing them with the type serums of the Lister Institute or of the Medical Research Committee.

Lumbar Puncture and Serum Administration. The needles used for lumbar puncture should fit an ordinary Record syringe or the metal attachment of the rubber tube which is used by those who prefer to introduce the serum from a funnel by gravity. The patient is usually placed on his left side with the knees well drawn up and with the head and shoulders bent forward as far as possible. The under arm should be pulled well forward. The puncture is made in the fourth lumbar interspace, which can be readily identified by the fact that a line connecting the summits of the iliac crests intersects the fourth lumbar vertebra. The skin in the neighbourhood is thoroughly cleansed and painted with iodine. The needle must be carefully sterilized and, especially at a first puncture when bacteriological results are of most importance, it is advisable for the operator to wear rubber gloves. The theca can be reached by two routes, *between the spines* or *between the laminae*. Of these the first is by far the easiest and, universally practised in the case of children, is equally applicable to adults. The interspinous ligament being firmly grasped between the finger and thumb of the left hand to prevent its being laterally deflected, the needle is inserted, exactly in the middle line and just above the lower spine, and pushed gently and firmly forward, either directly or with a very slight upward slant. After piercing the tough ligament, and for this purpose the needle should be both strong and sharp, one can usually feel a slight sensation of something giving way a little deeper in the back before the point of the needle as the dura is punctured. The stilette is then withdrawn and the fluid is collected first in sterile tubes

for examination and then in a graduated glass measure. The depth at which fluid is struck varies much with the age and size of the patient, say from half an inch or less in a small infant to $3\frac{1}{2}$ inches or more in a muscular or fat adult. Too deep a thrust is apt, by passing across the space and penetrating the venous plexus behind, to cause bleeding which, always unfortunate, is particularly annoying at a first puncture, as the blood prevents a definite decision as to whether the fluid is clear or turbid. For this reason, when puncturing very young infants I prefer to use an ordinary antitoxin syringe needle without a stilette so that, if the space is reached sooner than is anticipated, the spouting of the fluid at once announces the fact and avoids the risk of too deep a thrust.

If there is much pressure and, as not infrequently happens, the fluid spouts or comes out in a continuous stream, it should be checked by retaining the stilette partly in position, as the too rapid withdrawal of large amounts does not appear to be altogether free from risk. As a rule, if the process is not too hurried, it is safe to let the fluid flow until it exudes slowly, about one drop in three or four seconds. Amounts up to 80 and 90 c.c. are not infrequently obtained in the case of adults, and in one fatal case punctured on the second day 115 c.c. were obtained without difficulty. From a woman admitted comatose we withdrew 180 c.c. of clear sterile fluid, with the result that she was apparently well in two days and left hospital shortly after without the cause of the condition ever being explained. More common amounts in adults suffering from cerebro-spinal meningitis are from 50 to 70 c.c., and the quantity of fluid obtained remains much the same at subsequent punctures except in the so-called 'suppurative' cases, in which it usually decreases steadily. In children in the acute stage about 30 or 40 c.c. may be expected, while in chronic cases of hydrocephalus in infants this amount may be doubled or almost trebled in some instances.

If the puncture is to be made *between the laminae*, a point midway between the spines and a quarter of an inch external to the middle line is selected and the needle is directed inwards and slightly upwards. There is less resistance to be overcome in this route, and its advocates claim that it allows greater delicacy in manipulation. But it is certainly more difficult and should be avoided by beginners. If a syringe is used, moreover, for the introduction of the serum, it is thrown at rather an awkward angle for the injection, an objection which does not apply if the tube and funnel is used.

Occasionally fluid is not struck. This may be due merely to the blocking of the needle, which should be cleared with the stilette. Or the dura may have been pushed before the point of the needle and remained unpunctured. Or, again, the pierced membranes may have wrapped themselves round the

point, and rotating the needle may meet the difficulty. Adhesions, moreover, may have occluded the canal, though in this case a few drops of fluid usually exude. Lastly, the fluid may be too purulent and sticky to flow. Whatever is the cause of the difficulty, a 'dry tap' should always be regarded with great suspicion and the presumption always is that the theca has not been properly penetrated. It is advisable to try a higher space, and it may be remarked here that the second and third spaces seem to be as safe as the fourth. If it is believed that the fluid is too thick to flow, an attempt may be made to wash out the canal between the second and fourth spaces, two needles being inserted and saline solution injected into the upper one.

It is usually wise to give an *anæsthetic*, particularly if it is intended to inject serum. Many patients are delirious and cannot be properly controlled, and a needle broken in the back is a very awkward accident. Again, the daily treatment, if an anæsthetic is not given, becomes a real terror to the patient, as intrathecal injection causes a considerable amount of pain in the back and legs. Chloroform is, as a rule, excellently tolerated, but it is none the less wise to avoid anæsthetics in the case of infants, who can easily be held steady and who do not stand injection of serum at all well, both the pulse and respiration often giving cause for an anxiety which is only increased if chloroform is employed.

When any suspicious case is punctured antimeningococcal serum should always be at hand and, if the fluid is found to be turbid, the vial should be at once placed in hot water so as to be ready for use when the drainage of the canal is completed. It is obvious that the turbidity may afterwards be found to be due to septic or pneumococcal infection, but it would waste valuable time to wait for a definite bacteriological diagnosis. While it is true that unnecessary introduction of serum is not desirable, we can do no harm by injecting it in cases the outlook of which may be regarded as invariably hopeless, and the probabilities are always in favour of a turbid fluid being due to meningococci. If, however, clear fluid is obtained on puncture, unless the case is an extremely early one and the other conditions point very strongly to meningococcal infection, it is best to withhold serum which, theoretically, by causing a reaction in the meninges might determine the localization of infection in that situation, if the meningococci are already in the blood-stream. It is true that this theory does not receive any support from recent experiments on monkeys carried out by Amoss and Eberson, but perhaps the best procedure in such cases is the intravenous injection of serum followed by another test puncture after an interval of not more than twelve hours. In most instances, however, the patient with clear fluid can be safely left without serum. Perhaps of more practical importance than the

theoretical objection raised above is the fact that injection of serum obscures the diagnosis by setting up an aseptic meningitis and by causing a clear fluid to be distinctly turbid at a subsequent puncture.

I am accustomed to use the syringe for injection and have seen no reason to consider it dangerous if properly used, though many regard the

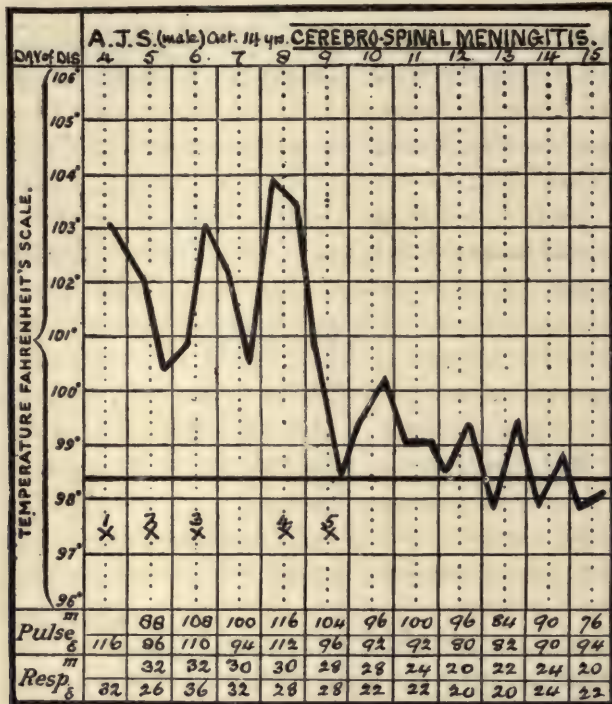


FIG. 63. Case treated with Flexner's serum: recovery. Note the termination by crisis. The numbered crosses indicate the spinal injections.

1. 34 c.c. turbid fluid withdrawn at 11.45 p.m.: 30 c.c. serum injected.
2. 21 c.c. fluid, less turbid, withdrawn at 8.15 p.m.: 30 c.c. serum injected.
3. 16 c.c. slightly turbid fluid withdrawn at 12.30 p.m.: 15 c.c. serum injected.
4. Exacerbation of symptoms; 30 c.c. turbid fluid at 3.30 p.m.: 30 c.c. serum injected.
5. 30 c.c. fluid, almost clear, at 8 p.m.: 30 c.c. serum injected.

N.B.—At puncture No. 1 diplococci both intra- and extra-cellular; at Nos. 2 and 3 all intracellular; at 4 and 5 no germs observed. Polymorphs only.

funnel and tube as a safer method. The syringe should be a well-fitting one and work smoothly. When filled it is joined to the needle, already in position, and the injection is made exceedingly slowly and with very even pressure, all jerking being sedulously avoided. It is not safe to inject at all rapidly even if large quantities of fluid have been withdrawn, and it is well to allow at least 10 minutes for the introduction of about 20 c.c. of serum. Sophian has

proved that there is always a slight *fall in the blood pressure* as the injection commences and that later a very sudden and decided fall occurs which he regards as indicating that further administration must cease. I am not accustomed to control my injections by blood-pressure observations, but have done so in enough cases to verify the fact reported by Sophian. But I none the less consider that a careful watch on the pulse and respiration during injection gives sufficient indication when to stop. The *accidents* reported as immediately following the introduction of serum have been attributed to an anaphylaxis and to increased intra-cranial pressure, and we may conclude with Flexner that the latter is the real danger of intrathecal injection. It is usual for the breathing to fail before the heart, and prompt artificial respiration will often save the patient. If a considerable amount of serum has been introduced, it is well to let some of it at least run out.

Dosage. The possibility of dangerous results following too large an injection makes it necessary to be careful in determining the dose. Only in very exceptional circumstances should it exceed the amount of fluid

withdrawn, but cases are occasionally met with in which so little fluid can be obtained that the cautious injection of a moderate dose might well appear to entail less risk to the patient than the withholding of serum. That the introduction of an excess of serum is compatible with a successful issue is shown in the charts (Figs. 63, 64), but both the patients concerned were treated as long ago as 1908, and I very seldom think it necessary nowadays to push the serum to the extent shown in the second chart (Fig. 64) and would be more likely to be content with doses of 15 or 20 c.c. at most. However,

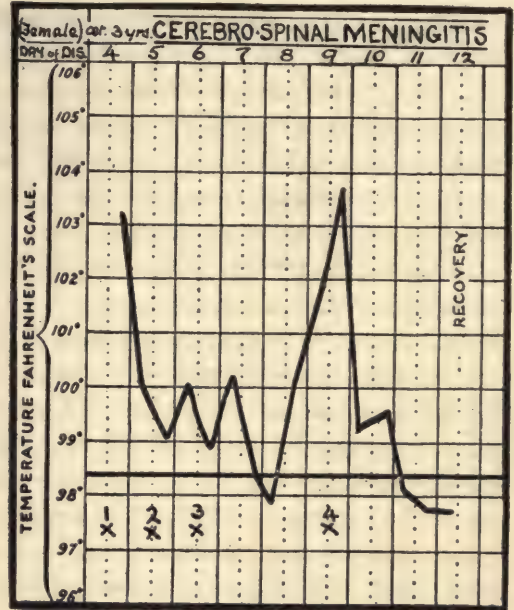


FIG. 64. Case treated with Flexner's serum. The numbered crosses indicate the spinal injections.

1. 20 c.c. very turbid fluid at 9 p.m.: 30 c.c. serum.

2. 2 c.c. very turbid fluid at 8 p.m.: 30 c.c. serum.

3. 18 c.c. turbid fluid at 7.30 p.m. 30 c.c. serum.

4. Recrudescence of symptoms. 40 c.c. turbid fluid at 3.30 p.m. 30 c.c. serum.

whether from a difference in the type of disease or, as is more probable, from a much greater experience of lumbar puncture, the amount of fluid obtained in recent years seems to have been on an average very much greater than in the 1908 cases.

The doses recommended by Sophian are smaller than those of other authorities, but his good results speak eloquently in favour of their efficacy, and, as I am always anxious to reduce pressure as well as to give serum, my own practice has been much influenced by his teaching. For infants 5 to 10 or, very exceptionally, 15 c.c. is a sufficient dose. It is doubtful, indeed, if there is much advantage in giving more than 15 c.c. in children under 5 years of age, though some will tolerate 20 and even 30 c.c. (Fig. 64) quite well. Doses of from 20 to 30 c.c. appear suitable for patients between 5 and 18 years, after which from 30 to 40 c.c. can be given safely in most cases. If, however, the puncture does not yield more than 40 c.c. I think it wise to be contented with 20 or 25 c.c. as a dose. On the other hand, even when very large amounts of fluid are withdrawn, I see little advantage in exceeding the amounts named above, which are only slightly in excess of those recommended by Sophian. Dopter disapproves of doses as small as 10 c.c. even in infants, and thinks that 15 c.c. should be the minimum. But in at least half a dozen cases respiratory difficulty and syncope have occurred shortly after the former amount was reached, although no anæsthetic was used and every care taken to inject slowly, and Sophian's results prove, to my satisfaction at least, that even doses of 5 c.c. are of therapeutic value.

The importance of the prompt administration of serum has been already emphasized. As in diphtheria, the earlier in the disease the treatment is started the better are its results. Equally vital is the necessity of *repeated injections* for some days. The practitioner must not be misled by improvements in the patient which may be only temporary (Figs. 63, 64). At least four consecutive injections, at intervals of not more than twenty-four hours, should be given in every case, and if micro-organisms persist in the fluid it may be necessary to inject for 6 or 7 days in succession. After the fourth day the *condition of the fluid* should be taken as a guide and, if diplococci are detected in the direct film or if they multiply in the incubated fluid, further treatment is necessary. When a patient is improving, the germs tend to become all intracellular, and a little later they are apt to stain badly and to become fragmented. The polymorph cells decrease in number, and a differential count shows a relative increase in lymphocytes and endothelials. Glucose, which is absent at first, can be detected in the fluid and increases in amount. The *condition of the patient* is not so safe a guide as is that of the fluid. On the one hand, the meningitic symptoms may appear more marked though the

fluid is improving; on the other, the patient may look very much better while the cytology and bacteriology of the fluid show that he is, in reality, worse. Nevertheless, disappearance of cyanosis, greater regularity of the respirations, and recovery of the consciousness suggest an improvement, and Flexner lays great stress on the subsidence of the temperature abruptly by crisis (Fig. 63).

After-treatment. When the injection is completed, the puncture is sealed with cotton-wool and collodion and the foot of the bed is raised on blocks for a few hours to encourage the flow of serum to the base of the brain. It has been suggested that the patient might maintain a ventral position during this time, so as to allow the optic chiasma to be more readily reached. The elevation of the foot of the bed may also be used while the injection is proceeding, and it is sometimes convenient to tilt the bed in the opposite way while the fluid is being drawn off. In this connexion it may be added that there is a possible disadvantage in always placing the patient on the same side for a puncture, as the lower ventricle is not well drained. At one autopsy I found the left ventricle lined with organized pus, whereas the right was quite free, and this patient had always lain on his left side for puncture. Since then I always see the head is raised for some minutes during the drainage; others might prefer to have the patient lying on sides alternately.

In cases in which the meningococci appear to be 'fast' to the serum, and the fluid remains turbid even after 7 or 8 injections, the best plan is to stop the administration of serum but to continue drainage at frequent intervals, if not daily.

In infants in whom, owing to *blockage of the foramina*, lumbar puncture fails to relieve the ventricles, an attempt may be made to puncture and *inject through the fontanelle*, the needle being inserted at the lateral angle and pushed gently through the brain substance. Successes have been reported, but when adhesions have occurred in one place it is more than likely that they have done so in others, and the circulation of the serum through the cavities of the brain may be prevented. I have had no good fortune in the few cases in which this procedure has been adopted. Trephining operations have been performed in older persons, but for the same reason too much must not be expected of them.

Intravenous injections. Herrick, believing that the disease originates as a generalized meningococcus sepsis, has modified the ordinary procedure of serum therapy by supplementing the intrathecal by intravenous injections. If the fluid is found to be turbid, serum is given in the usual way; if it is clear, no intraspinal injection is made. A desensitizing dose of serum is

given in case of accident and an hour later from 50 to 100 c.c. are injected into a vein. These injections are repeated every twelve hours until the

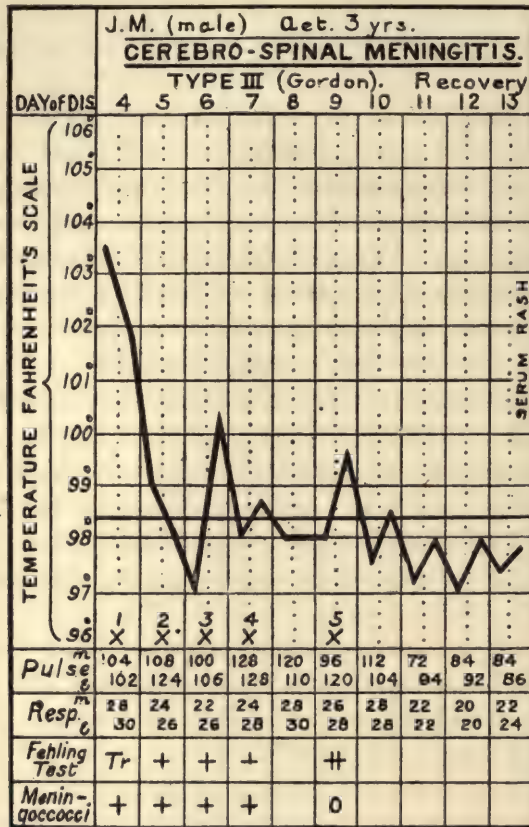


FIG. 65. A case treated successfully with the Medical Research Committee's Type Serums. The numbered crosses indicate the intrathecal injections.

1. 42 c.c. turbid fluid withdrawn at 4.30 p.m. : 20 c.c. serum, pooled Types I and II.
2. 33 c.c. turbid fluid at 1.10 p.m. : 15 c.c. serum, pooled I and II.
3. 45 c.c. opalescent fluid at 1 p.m. : the group reaction I-III having been determined by the rapid method, 15 c.c. Type I serum injected.
4. 46 c.c. slightly opalescent fluid: the type having now been definitely distinguished as III, 15 c.c. Type III serum (see Table K).
5. 45 c.c. clear fluid: 15 c.c. Type III serum.

In this case improvement was noted from the first and before the correct type was used. Note increase in glucose. Organisms still present in direct smear at fourth puncture; at fifth no meningococci in smear or culture.

temperature is normal, or until 6 to 8 injections have been given. If meningitis develops, the spinal canal is very thoroughly drained and sufficient serum

is injected to relieve the headache which results from the drainage. Herrick's view is that the drainage encourages the passage of antibodies from the blood through the choroid plexus. In this connexion Amoss and Eberson state that serum introduced into the subarachnoid space soon begins to escape into the blood and that for this reason repeated intrathecal injections are necessary to keep the meninges bathed in the serum. The passage of the curative serum into the blood leads to its general distribution through the organs. The greater concentration in the blood, when intravenous injections are practised, should be of assistance in overcoming meningococæmia. They conclude that after spinal injection the agglutinins disappear from the fluid in 12 hours and appear in the blood in four hours but quickly diminish. After intravenous injection agglutinins appear in the spinal fluid in small amounts after twelve hours and increase to the 25th hour. After combined spinal and intravenous injection the agglutinins remain in higher concentration in the spinal fluid and for a longer time than by either of the other methods. The agglutinins remain in maximum concentration in the blood for twenty-five hours. It appears, then, that this very valuable scientific work is in complete accord with Herrick's clinical observations. It has been so recently published that I have had no opportunity of applying its conclusions to my practice, but I think perhaps the most important lesson to be derived from it is the necessity of early repetition of intrathecal injections, especially if intravenous injections are not given. I have frequently given the second injection about twelve hours after the first, and, if it is a fact that the agglutinins have disappeared from the fluid by that time, it would seem that this should be done in all cases. As regards intravenous injections I have hitherto reserved them for septicæmic cases and have not repeated them as often or with as large doses as Herrick advises. In this particular, too, a revision of our present methods would appear desirable.

Treatment with Type Serums. The recognition of the agglutinative differences of different strains of meningococci inevitably led to an attempt to treat the patient with a serum appropriate to the type of his micro-organisms, and latterly the requisite type serums have been available for this purpose. I have used both those prepared at the Lister Institute and those of the Medical Research Committee, 'M.R.C.' serums. The procedure adopted is to start the injections with either a polyvalent or a pooled serum and, when the type is distinguished by the usual agglutination tests, to continue the treatment with the appropriate monotypical serum. The so-called 'pooled' serum of the Medical Research Committee consists of equal quantities of serum from horses immunized respectively

against Type I and Type II meningococci. The serum, then, is effective against both main groups of meningococci, and, even in those cases in which, from want of sufficient growth on culture, typing has been impossible, it has in my hands given satisfactory results, a fact which tends to support Sophian's views regarding the efficacy of moderate doses, as it is obvious that the patient only profits by half the nominal dose which is administered. When type serums are to be given it is well to make several cultures, with a view of securing as early as possible a sufficient amount of growth to make the necessary emulsions for performing the agglutination tests. These are carried out with the four type serums now procurable by the macroscopic sedimentation method in small test-tubes as in enteric fever. A more rapid and fairly accurate method is to mix a drop of emulsion with a drop of diluted serum on a glass slide, and by this means time may be saved as very little growth is required. In the chart (Fig. 65) the treatment of a case is illustrated as an example. The appended table shows the agglutination reactions of two cases of which J. M. is the one in the chart referred to.

TABLE K
AGGLUTINATION TYPING OF MENINGOCOCCI

Case.	Type.	Dilutions.				Result.
		$\frac{1}{100}$	$\frac{1}{200}$	$\frac{1}{400}$	$\frac{1}{800}$	
J. M.	I	+++	+++	++	+	} = Type III
	II	—	—	—	—	
	III	+++	+++	+++	++	
	IV	—	—	—	—	
M. N.	I	—	—	—	—	} = Type II
	II	+++	+++	+++	+++	
	III	—	—	—	—	
	IV	+	+	—	—	

While it may be admitted that treatment on these lines is desirable in every case, I cannot say that so far the use of type serums has improved my results, the mortality being very similar to that of cases treated with polyvalent serums. Indeed, it is common to observe considerable improvement with the pooled or polyvalent serum which has to be used before the type has been identified, or, again, death may occur before identification is established. It seems to be generally agreed that it is more difficult to secure a satisfactory monotypical serum against Type II meningococci. As regards the M.R.C. serums in particular, while Type I cases have done well, those of Type II have done uncommonly badly. It has been suggested that still further differentiation of this type, of which there appear to be three subvarieties, will be necessary for successful treatment, and that a

pooled Type II serum, prepared by the mixing of the serum of horses individually immunized against the subvarieties, might give better results. In the meantime I must confess that I would almost prefer to use a polyvalent serum throughout, provided it was of established reputation such as Flexner's.

Although it has been said that Type I is more virulent as regards the meninges, and that Type II is more associated with meningococæmia and metastases and is on the whole less fatal, the question is very much obscured by the efficiency of the serums employed in treatment. H. D. Rolleston found that in a small outbreak of cases of Type II the meningitis manifestations were very severe, and I have had the same experience. It may be mentioned here, although the point is of no practical importance, that, whereas in England and France Types I and III (Nicolle's Group A) are regarded as the meningococcus, Flexner, Olitzky, and others appear to consider that group as the parameningococcus.

Serum Sickness. As in the case of diphtheria, we must expect a certain proportion of our cases to suffer from the serum disease. Although a high percentage of my own cases, 77 per cent. in recent years, have manifested serum sequelæ, there is not much evidence that intrathecal injection is responsible for such a result, as percentages quite as high were not infrequently noted in the early days of subcutaneous injection of anti-diphtheritic serum. I am inclined to attribute the frequency of serum sickness to some differences which may be reasonably supposed to exist in the preparation of the serums, special precautions with a view of diminishing serum sequelæ having been for long practised by the firms which supply diphtheria antitoxin. In any case serum sickness occurs frequently in meningitis and usually shows itself about the ninth day after the first injection. The rashes are often prolonged and severe, and have been accompanied by pyrexia more frequently than has been my experience in diphtheria wards. Arthritis is not uncommon, and must be distinguished from that which occasionally complicates the disease itself (Fig. 66).

The practical importance of the serum disease is that its onset is liable to be mistaken for a recrudescence of meningitis. The intrathecal injection of serum sets up a reaction of the meninges, an aseptic meningitis, which may convert a clear fluid into a turbid one. Headache, temperature, and increased rigidity not infrequently appear just before the rash and may well occur without a rash at all. In such a case to resume serum injections is probably unwise, although I have often done so without bad results before the nature of the condition was realized. But assuming that a fluid previously reported clear has once more become opalescent, or actually turbid,

the presence or absence of the power to reduce Fehling's solution will throw light upon the question. Reveillet, Nové-Jusserand, and Langeron suggested this method of distinguishing meningism or aseptic meningitis from the actual disease. They recommend the use of a diluted Fehling's solution (1-4) and boil 4 c.c. together with 10 c.c. of the suspected fluid at the bedside. If sugar is present there is no need to give serum. I find I get excellent results with only 1 c.c. of the diluted Fehling's solution to 10 c.c. of fluid, a normal fluid giving a definite orange cloud on boiling. Provided meningitic symptoms continue and the fluid is found sterile, treatment should consist of lumbar puncture at suitable intervals.

Results of Serum Treatment. While we can never say with any certainty that a given case will improve after serum injection or that a particular serum can be relied upon to give good results in all cases, uncertainties which depend on the type of the infecting organism and the presence or absence of its homologous antibodies in the serum used, there is no doubt that the intrathecal injection of serum has been proved successful and is, at present, the rational way of dealing with the disease. This success we owe chiefly to Flexner. His statistics, compiled in 1913, show that by that time 1,294 cases had been treated with his serum with a mortality of 30.9 per cent., and that deafness and other serious sequelæ of the disease occurred very seldom. In the 1907-9 outbreak our hospital mortality in Edinburgh was reduced from 80 to 37 per cent., and even better results were obtained by Gardner Robb in Belfast. Although the serums available during 1915 did not appear suited to the type of meningitis then prevalent, from 1916 onwards several were obtainable which gave quite good results. My results with Flexner's serum in 1916-17 were very satisfactory, a consecutive series of 60 cases giving a mortality of just 26 per cent. Slightly less than half these cases were soldiers and sailors who had a case death-rate of under 15 per cent., a figure which corresponds with that given by Dopter for the French army. But in 1918 a different type of infection, more resistant to Flexner's serum, seemed to prevail and, by the time 17 more cases had been treated, the mortality for the 77 had risen to 35 per cent. These cases, added to the 53 treated with the same serum in 1907-9, give a total of 130 with a case death-rate of 36 per cent. With the unreliable serums of 1915 the City Hospital mortality was 50 per cent. Thereafter with the Lister, Flexner, and M. R. C. serums the death-rate was 36 per cent. in 125 cases in all. These figures include all deaths, even if they took place within half an hour of the first injection of serum, and of course differ from military statistics in comprising persons of both sexes and all ages. The disease is particularly severe in young infants, and 18 of the last 20 admitted

to hospital died, not only on account of the susceptibility natural to their age, but because they did not for the most part come early under treatment. Chronic cases admitted one and two months after the onset were not uncommon, and have unfortunately to be included. It may be mentioned here that the patients treated with type serum, either Lister or M.R.C., had a death-rate of 33 per cent.

Vaccine Treatment. In very acute cases vaccines would not appear to have much chance of success, but it is reasonable to use them for patients who are tending to become chronic or who are suffering continual reinfections from some focus in which micro-organisms persist and are, by reason of adhesions or from some other cause, out of the reach of serum. MacLagan speaks favourably of vaccines and recommends doses of from 50 to 100 millions, to be repeated and increased at intervals of from 3 to 5 days. Other authorities have used smaller amounts, and, in conjunction with other treatment, the results obtained have been encouraging. The vaccines are, as a rule, autogenous, but, if a stock vaccine with a reputation for promoting the formation of antibodies could be procured, I should be inclined to prefer it. In one chronic case in which six distinct attacks occurred in six months, the fluid being clear and sterile in the intervals and the patient well enough to be discharged on two occasions from hospital, a course of autogenous vaccines in moderate, 17-50 million, doses, given during the last relapse, was probably the means of finally overcoming the infection.

Treatment of Convalescence and Complications. I find it advisable to keep even mild cases in bed for three weeks and to forbid any exertion for some time afterwards. During convalescence the patient should be most carefully watched, and any unexpected rise of temperature, onset of headache, or access of vomiting should be regarded as an indication for immediate lumbar puncture. The chronic stage of the illness, with its emaciation and distortion, appears to be directly due to hydrocephalus, and care must be taken to prevent this condition becoming established (Fig. 66). Nevertheless it is wise in these cases not to drain the canal too completely, as too frequent and too thorough drainage appears to lead to the more rapid secretion of cerebro-spinal fluid. I remember one small baby from whom 100 c.c. were withdrawn twice daily for about a week and, although the case would have been fatal in any circumstances, it seemed to me the secretion of fluid was actually encouraged by the treatment. An adult male, again, who complained of intense headaches and from whom 80 or 90 c.c. were daily withdrawn, commenced to improve when the punctures were made at two-day intervals and when it was determined not to draw off more than 60 c.c. at a sitting. General tonics and, in my experience, malt

liquors appear to do the patient good. Lying out in the open air and plenty of good food also seem to restore the nervous tone.

As regards complications there is little to be said. Nothing can be done for nerve deafness or for the iridochoroiditis and other serious eye conditions which occasionally occur. Arthritis may be relieved by hot

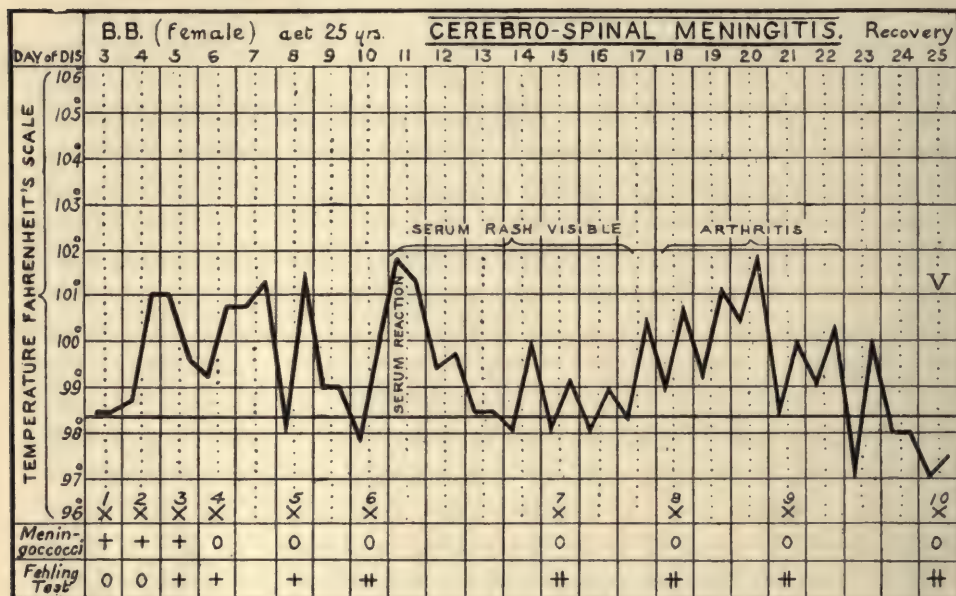


FIG. 66. Case treated with Flexner's serum and thereafter with lumbar punctures—Recovery.

The numbered crosses indicate lumbar punctures, and the first six were followed by the injection of 20 c.c. doses of Flexner's serum. The remaining punctures were performed for threatened hydrocephalus, intense headache being the indication for 3 of them and giddiness and vomiting for the last. Note also the serum reaction. The subsequent arthritis followed it so closely as to be in all probability due to the same cause and not meningococcal. The definite presence of sugar is indicated by +, the normal by ++. Had the fluid which was opalescent with the onset of the reaction been tested at the bedside, serum would not have been given.

applications, and, if the joint becomes tense, aspiration is a useful measure. Should the fluid contain meningococci and show signs of again collecting, the best treatment is injection of serum into the cavity of the joint, the patient, if necessary, being first desensitized in the usual manner.

PROPHYLAXIS. The patient must be first dealt with, and his **isolation**, preferably in hospital, is advisable. Except for naval cases it has not been our custom in Edinburgh to obtain negative swabs from the naso-

pharynx before discharge, and it is probable that in very few instances does the meningococcus persist for the time that a patient's illness keeps him in hospital. But it is certainly advisable to obtain negatives before allowing men to return to crowded ships or barracks. As regards contacts **quarantine** appears unnecessary, but swabs should be taken and, when possible, detected carriers should be actively treated, if not isolated.

Remembering the factors which predispose to the disease, when it is desired to prevent or limit the spread of meningitis in barracks and institutions our first duty is to *avoid overcrowding*.

Glover, whose interesting observations on the relationship of overcrowding to outbreaks of the disease have made him a recognized authority on this question, found that the 'spacing out' of the beds in barracks was at once effective in limiting infection. Severe overcrowding when beds are only one foot apart is accompanied by a 'high carrier rate', at least 20 per cent. Moderate overcrowding is associated with a lower rate, say from 10 to 20 per cent., whereas a carrier rate of from 2 to 5 per cent. may be considered usual under the best conditions obtainable in barracks and huts. 'Quite a moderate degree of "spacing out" of beds combined with simple methods for improving ventilation are highly efficient agents in reducing high carrier rates. When a unit shows a high carrier rate, a distance of at least two and a half feet between beds should be enforced.' A reasonable procedure to adopt with troops, then, is to occasionally test a sample, say 100 men, of a unit to discover what proportion of its men are carriers and to act accordingly. A high rate, over 20 per cent., is an index which heralds the appearance of cases. When it is detected active measures in the way of spacing out will probably prevent the outbreak.

It will be noticed that Glover mentions the importance of free *ventilation*. All of us who have worked with troops have noted their rooted objection to open windows. Arrangements can, however, be made for fixing windows in such a manner that they cannot be completely shut. He also observed that the depression left by inoculation, when taken together with the change of conditions of life of the new recruit, seemed to predispose, and advises its postponement until the second month in barracks.

Care should be taken to avoid the common use of handkerchiefs and towels. *Disinfection* does not appear a very necessary measure in the case of a disease with a virus so delicate. In barracks some supervision of the washing of cups and glasses, especially in the canteens, is desirable, and everything should be done to discourage indiscriminate spitting.

Treatment of Carriers. There is some difference of opinion regarding the question whether it is necessary to segregate and disinfect carriers,

and the German writers generally consider such a procedure useless. But it is probably a wise precaution to take in the case of troops. It is often difficult to rid the carrier of his germs. It is advisable he should be in the open air as much as possible and the nasopharynx should be sprayed at frequent intervals with some disinfecting solution, such as permanganate of potash 1-1,000, or zinc sulphate 1 per cent. I have usually used a solution consisting of iodine 5 drachms, guaiacol half a drachm, and thymic acid 4 gr. in 8 ounces of rectified spirit, but I have little faith in it or any other preparation. The patient probably gets rid of his micro-organisms independently of treatment. The steam spray, with the jet devised by Hine, affords the most suitable method of dealing with large numbers of persons at once, and the steam may be medicated with sulphate of zinc or chloramine T. Since fitting a room with this apparatus at the City Hospital all carriers sent to us have been treated by this means, but the same proportion of resistant cases appear to occur. There is some evidence, however, that the method is reasonably effective in the great bulk of cases, and it forms by far the most convenient mode of treatment, as the installation can be made to accommodate almost any number of patients at once. Fildes and Wallis state that 30 per cent. of carriers are cured spontaneously with any or no treatment and that no antiseptic has any particular advantage over another.

Preventive Vaccination has been practised by Sophian, Greenwood, Gates, and others. It is very doubtful if protection of this sort is required in the case of a disease of such low infectivity. Doses of from 500 to 8,000 million organisms have been given, usually in three injections at weekly intervals. It is probable that a considerable degree of immunity may be acquired in this way.

CHAPTER XV

FEVER HOSPITAL PROBLEMS

Difficulties of Fever Hospitals.

Coexistence of Infectious Diseases.

Cross Infection, so called, in Fever Hospitals :
cubicle, barrier, and bed isolation systems.

Aggravation of disease by superadded septic
infection.

'Return Cases.'

THERE are difficulties associated with the aggregation of large numbers of patients in fever hospitals which, to some extent, have impaired their usefulness, and have in certain quarters caused a feeling of distrust regarding their success. It had undoubtedly been hoped that, with the compulsory isolation of a large percentage of the infected sick, a much greater diminution in the spread of infectious disease would have been observed than has been actually the case. But it must be remembered that recent improvements in sanitation, in public health administration, and in hospital isolation have coincided with the appearance of new conditions which render the spread of infection a much easier matter than it used to be in the past. Thus, increase in the facilities of movement from place to place, cheap excursions, multiplication of cars, omnibuses, and light railways, and, perhaps above all, compulsory education, with its herding together of even very young children in large classes, have done much to counteract any good results which could be expected from modern preventive methods. It is unnecessary to condemn fever hospitals because hitherto they have not been the success which was expected. They are improving constantly in their construction, their administration, and their methods of treatment, and will, doubtless—for we are always learning—ultimately fulfil the aspirations of those who originally recommended them as a means of effectively controlling epidemic disease.

While, no doubt, the primary object of a fever hospital is isolation, it must not be forgotten that the care of the patients themselves is a matter of supreme importance. And in this I think there is little sign of failure, as the following figures, relating to the mortality from infectious diseases in Edinburgh for a period of five years, will show. It will be noticed that for all the notifiable diseases the hospital mortality is lower than that of

the total mortality in the city, including that of the hospital. The table is constructed on the uncorrected notifications. It may be urged that the numbers are small, and that there is always a possibility of very bad cases terminating fatally before they can be removed to hospital. It cannot, of course, be denied that this may occasionally happen, particularly as regards laryngeal diphtheria, but it must also be recollected that many patients die within twenty-four hours of their admission, and there is little reason to believe that the worst cases are treated outside. On the contrary, there is a distinct tendency to send in patients who, if only moderately ill, would be kept at home. Again, the percentage treated outside consists

TABLE L

ABSTRACTED FROM THE REPORT OF THE MEDICAL OFFICER OF HEALTH
OF EDINBURGH FOR 1907

Years.	Percentage mortality of all cases in City, including the Hospital.					Percentage mortality of cases treated in Hospital.				
	1903.	1904.	1905.	1906.	1907.	1903.	1904.	1905.	1906.	1907.
Scarlatina . . .	3.74	2.89	1.80	3.44	2.16	3.01	2.33	1.47	2.94	1.99
Diphtheria . . .	10.26	8.37	9.05	7.19	5.03	7.40	6.57	7.25	4.95	3.40
Enteric Fever . .	9.28	11.22	9.52	8.20	10.68	6.95	9.32	4.45	3.65	7.40
Erysipelas . . .	3.45	4.24	8.61	7.41	3.33	3.20	1.97	6.71	8.64	2.94

N.B.—The percentage of hospital treated cases for the four diseases was as follows :

Scarlatina,	from 83 % to 92 %, average about 88 % for 5,414 cases.
Diphtheria, ..	74 % to 85 %, 80 % .. 3,303 ..
Enteric Fever, ..	85 % to 91 %, 88 % .. 891 ..
Erysipelas, ..	35 % to 50 %, 43 % .. 1,715 ..

entirely of patients for whom isolation accommodation satisfactory to the Medical Officer of Health can be obtained at home ; in other words, those treated in the town are probably the best fed, the best clothed, and the least neglected. For other infectious diseases the figures no doubt would be different, as, indeed, they were when measles was a notifiable disease in Edinburgh. The measles and whooping-cough patients admitted to hospital form only a small percentage of the total in the city, and are almost exclusively from the poorer quarters. Moreover, a large proportion have complications on admission, and are probably sent in for that reason. The hospital death-rate under such conditions cannot fail to be greater than that for the whole town.

The main charges made against fever hospitals are three in number. It is said that firstly a patient often contracts another infection, secondly that his own illness may be made worse by his association with severe cases of the same disease, and thirdly that the isolation does not effect

its object, as, after discharge from hospital, he often carries the infection to others. No one would deny that there is truth in all these statements. They are, in any case, worthy of being considered in some detail. First, however, it will be well to enter briefly into the subject of the coexistence of different infectious diseases in the same person.

COEXISTENCE OF INFECTIOUS DISEASES. For long a comfortable doctrine was held that an attack of one infectious disease, while it lasted, protected against another. This is, of course, entirely erroneous. Not only is the patient who is convalescing from certain infectious diseases particularly susceptible to attacks of others, but not infrequently two or more infections will run their acute course concurrently. It is, doubtless, probable that differences of susceptibility towards various infections are shown by different diseases. The diphtheria patient, for instance, seems very liable to take scarlatina. The enteric patient, on the other hand, almost seems to possess some degree of immunity towards that disease.

It is unnecessary to enter into all the combinations which may be from time to time observed. I constantly see cases in which two infections are present in the same patient. A very common combination is that of scarlatina and diphtheria, and a considerable number of patients are admitted annually to the Edinburgh City Hospital with both these diseases present in an acute stage. The liability of the scarlatina convalescent to develop diphtheria has been emphasized elsewhere (see p. 127). Measles and scarlatina may also coexist from the first. The chart (Fig. 67) shows

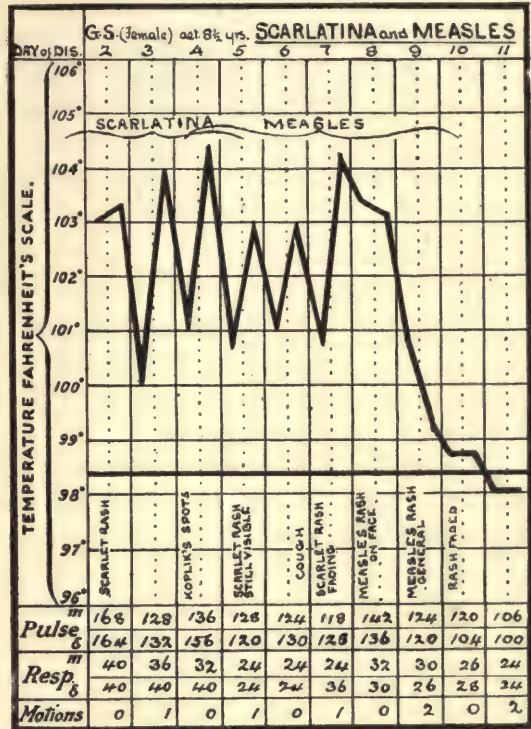


FIG. 67. To illustrate coexistence of infectious diseases. The patient was exposed to both infections. Admitted with typical scarlet fever. Two days later Koplik's spots appeared in the mouth. Coughing and coryza followed. Measles rash ultimately appeared. Note the typical measles crisis. Characteristic scarlatinal desquamation. Recovery.

an instance of their concurrence. The patient whose case it illustrates came from a school class which, at the time, was supplying us with both scarlatina and measles cases, and, with one of her companions, was unfortunate enough to contract both infections at once. It will be noticed that the scarlatina obtained a slight start, and that the measles eruption, developing a day or two later, caused the febrile period to be somewhat prolonged and influenced the character of its defervescence. Convalescents after measles or scarlatina readily contract the other infection. Another quite common concurrence is that of scarlatina and chicken-pox. Even allowing for the occasional difficulty caused by the presence of scarlatini-form rashes in the latter disease, it is by no means unusual to see both eruptions existing at the same moment on the same patient. Scarlatina, again, is frequently present in children suffering from the catarrhal or paroxysmal stages of whooping-cough. Lastly, as has been noted above (p. 112), scarlatina and enteric fever may occasionally, if rarely, coexist. It is a curious fact, however, that none of the hundreds of susceptible children who have passed through our enteric wards have ever contracted scarlatina in their convalescence.

The coexistence of measles and diphtheria is not rare, and, as is well known, the measles convalescent readily contracts the latter disease, the converse being also the case. It is quite common to see measles and whooping-cough run concurrently, and the development of the paroxysmal stage about a fortnight after the measles rash suggests that in many cases both infections are contracted practically at the same moment. Measles and chicken-pox is also a common combination.

Whooping-cough and diphtheria frequently coexist, and the whooping-cough convalescent contracts all the other infections readily if exposed to them. Erysipelas may complicate small-pox, enteric, or scarlatina; and mumps may be found in conjunction with almost any other infection.

In rarer instances three or more diseases may be present at once. The chart (Fig. 68) shows a case in which the chicken-pox eruption, appearing before a measles rash had faded, was still present when that of scarlatina appeared. I have seen combinations of scarlatina, chicken-pox, and whooping-cough; of scarlatina, mumps, and whooping-cough; of scarlatina, measles, and whooping-cough; and of four infections concurrent, scarlatina, diphtheria, chicken-pox, and whooping-cough. And even larger groups of coexisting diseases have been reported.

CROSS INFECTION, SO CALLED, IN FEVER HOSPITALS. It has been made a reproach against fever hospitals that the patients admitted to

them too often contract a disease other than that from which they originally suffered. The real causes of this are, I think, very imperfectly understood, the popular impression, shared by many medical men, being that infection is carried by the staff from one ward to another. Such an occurrence is, in my experience, extremely rare, the cause of the second infection being in the vast majority of cases imported into the ward from

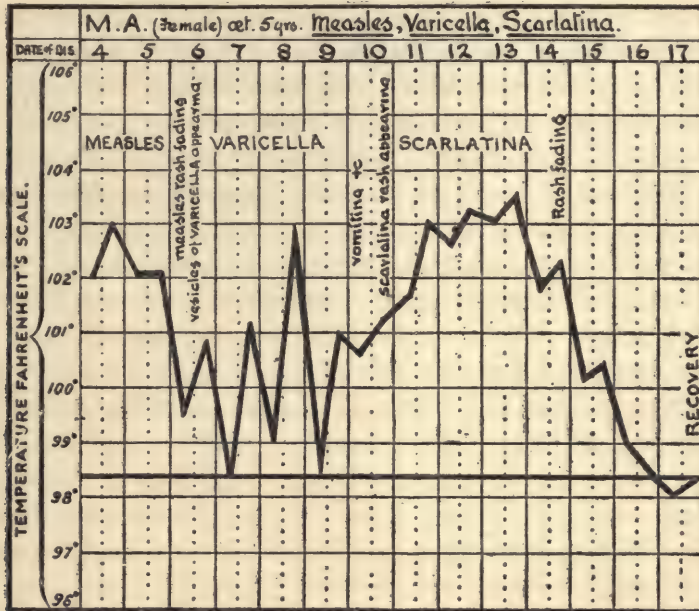


FIG. 68. Illustrating coexistence of infectious diseases. The patient admitted with good measles rash on the fourth day of an ordinary attack. As the rash faded chicken-pox vesicles appeared on the sixth day. The vesicles were still appearing on the tenth day, when scarlatina developed. It is probable that this last disease was contracted in hospital. Characteristic desquamation followed.

outside the hospital altogether, and brought in by other patients in one of the following ways.

In the first place, infection may be imported by a case being wrongly diagnosed by the patient's own medical attendant, and presenting at the time of admission no symptoms by which its true nature can be recognized. Thus a patient who is notified as diphtheria may have in reality scarlatina, but no rash being visible on admission, and no desquamation having commenced, the condition may be quite unrecognizable. No doubt all cases of this sort should be isolated, but isolation accommodation is not always sufficient, and it must be remembered that many true cases of both

scarlatina and diphtheria are unrecognizable at the time of their admission to hospital, and yet ultimately by their desquamation or by their paralysis prove the correctness of the outside diagnosis. If all such cases are isolated as a routine, it will be found that in most hospitals isolation accommodation will soon run short. In the year 1907 no less than seven cases of scarlatina were notified as diphtheria and admitted to the Edinburgh City Hospital. Most of them were sufficiently suspicious to be isolated on admission, but two were only recognized when they began to desquamate in the diphtheria wards, and one of these infected other children.

Secondly, a patient may suffer from two diseases concurrently, let us say, for instance, from scarlatina and diphtheria, and only one of these infections may be recognized. Diphtheria, for example, may be very obvious. The scarlet rash, on the other hand, may have disappeared before the medical attendant sees the case. Here again the true nature of the case may not be recognized till desquamation appears, and, in the meantime, the patient, if treated in a diphtheria ward, may cause an outbreak of scarlatina. Obviously both the outside medical attendant and the hospital authorities may be to blame for missing one of the two infections, but the difficulties are often extremely great, and, when one illness is obvious, the possibility of another coexisting with it is apt to be forgotten.

Thirdly, and this is the most insidious of all the ways in which infection is introduced from without, a patient may be admitted in the acute stage of one disease, and, at the same time, be in the incubation stage of another. Unless the second infection actually exists in the patient's home, the hospital authorities are not likely to hear of his exposure to it. A case of scarlatina, then, may be admitted. Before his admission he has been exposed to the infection of, let us say, measles or chicken-pox, both diseases in which the latent stage is a long one. Five or six days, or even a fortnight, after his admission the second disease develops, and infection is often spread to others before the patient can be isolated. An instance of this will be seen in Fig. 68, a patient admitted with measles developing a chicken-pox eruption a few days after admission.

It must be of course admitted that infection may be carried from ward to ward by the staff, if proper precautions are not taken, and we must remember the possibility of a member of the staff sickening with some infectious disease when on duty. But my experience has been that when an outbreak of a second infection occurs in any of our wards it is nearly always satisfactorily traced to one of the causes given above. Indeed, when we consider that in hospitals which do not admit cases of measles, rubella, chicken-pox, and mumps, as does the Edinburgh City Hospital,

exactly the same difficulties as regards these particular diseases occur, it is fairly obvious that the second infection is imported from without. In children's hospitals, again, the same problem is always present, and I am constantly admitting to our wards children who have become infected in the admirably managed Children's Hospital of Edinburgh.

The fact is, that wherever large numbers of children are aggregated together, whether in schools, in children's hospitals, or in fever hospitals, outbreaks of infection are bound to occur. The two causes first mentioned may to some extent be obviated by the free use of isolation wards, if these are available. As regards the third, the ambulance nurse should at least obtain information as to whether the patient has been exposed to any other infection. Care regarding this point will often reduce the amount of imported infection, though it will never stop it altogether. I find it a good plan not to allow patients to go to convalescent wards until three weeks have elapsed after their admission to hospital. As this period covers the incubation stage of all diseases except mumps, such a precaution at least saves the occupants of convalescent wards from imported infection, and the only disease which I see in such wards is post-scarlatinal diphtheria, another fair proof that infection is not carried from ward to ward by the staff.

Any ward in which a second infection breaks out must be quarantined and the infected person promptly isolated. Whenever possible it is a good plan to separate the contacts in groups of small numbers in small wards. It is possible that one or more groups may escape completely and thus avoid a second exposure.

We have seen on a previous page that outbreaks of diphtheria after scarlet fever, and we may add here after any disease, are not due to any of the above-mentioned causes, but depend almost certainly upon the presence of carriers in the wards. Our experience in Edinburgh is that from 10 to 15 per cent. of scarlet fever patients harbour the bacillus in the throat on admission. Even special wards provided for carriers have not, however, stopped the occurrence of diphtheria, probably because our laboratory resources, or want of them, have compelled us to be content with one negative from the throat, in itself a very insufficient safeguard, and we are obliged to ignore the nose altogether. There has been, therefore, ample opportunity for carriers to remain undetected. I find the best protection lies in the routine administration of a moderate dose of serum to every patient who suddenly develops the slightest patch on the throat or discharge from the nose. If this is done at once, the throat is usually clean before the almost inevitable 'positive' report comes back, and fatalities are practically unknown. The slightest suggestion of croup should be treated in the same way.

It may be of interest to give the statistics of the Edinburgh City Hospital for the year 1907 regarding the above points. Except that in some recent years more scarlet fever patients have taken diphtheria, or more precisely what may be called bacteriological diphtheria, and that the results as regards measles, rubella, and chicken-pox obviously vary with their epidemicity, the table gives a fair idea of our experience. The number of patients to contract a second infection has remained roughly at 1 per cent.

TABLE M

SHOWING IMPORTED INFECTION AND ITS RESULTS IN THE EDINBURGH CITY HOSPITAL
FOR THE YEAR 1907

I. INSTANCES OF WRONG DIAGNOSIS AND NOTIFICATION.

7 cases notified as Diphtheria were in reality Scarletina.					
2	"	"	Measles	"	"
2	"	"	Scarlatina	"	"
Many	"	"	Measles	"	"

II. DISEASES CONCURRENT ON ADMISSION.

2 cases admitted with Diphtheria			had concurrent Scarletina.		
2	"	"	Diphtheria	"	Whooping-cough.
14	"	"	Scarlatina	"	Diphtheria.
6	"	"	Scarlatina	"	Measles.
12	"	"	Scarlatina	"	Chicken-pox.
3	"	"	Scarlatina	"	Whooping-cough.
2	"	"	Enteric Fever	"	Scarlatina.
2	"	"	Measles	"	Scarlatina.
1	"	"	Measles	"	Chicken-pox.
1	"	"	Measles	"	Diphtheria.
13	"	"	Measles	"	Whooping-cough.
4	"	"	Whooping-cough	"	Chicken-pox.
2	"	"	Whooping-cough	"	Diphtheria.

III. CASES ADMITTED IN INCUBATION STAGE OF A SECOND INFECTION

2 cases of Diphtheria			admitted incubating Scarletina.		
3	"	"	Diphtheria	"	Measles.
2	"	"	Scarlatina	"	Measles.
3	"	"	Scarlatina	"	Chicken-pox.
1	"	"	Whooping-cough	"	Measles.
5	"	"	Whooping-cough	"	Chicken-pox.

IV. RESULTS OF ABOVE INTRODUCTION OF INFECTION.

4 cases of Diphtheria			took Scarletina.		
2	"	"	Diphtheria	"	Measles.
6	"	"	Scarlatina	"	Measles.
4	"	"	Scarlatina	"	Diphtheria.
5	"	"	Scarlatina	"	Whooping-cough.
4	"	"	Scarlatina	"	Chicken-pox.
3	"	"	Measles	"	Scarlatina.
1	"	"	Measles	"	Rubella.
1	"	"	Whooping-cough	"	Diphtheria.

Thirty patients in all, then, contracted a second infection. The total admissions to hospital were 3,560, so the percentage rate of infection was 0·84, not a very alarming figure when we consider the frequency with which children are daily exposed to infection in schools, in tramcars, in crowds, and in children's hospitals. The fever hospital cannot claim any immunity from the ordinary risks of infection. The numbers of patients treated in the principle wards were notified as follows: scarlatina 1,039, diphtheria 546, measles 870, whooping-cough 410, enteric 91, rubella 43, erysipelas 152, cerebro-spinal fever 122, chicken-pox 27, and phthisis 130. Nearly 2 per cent. of the scarlatina patients, it will be noticed, contracted a second disease, while for diphtheria the percentage was only just above 1, and for measles less than 0·5 per cent. We usually notice that any overcrowding is liable to increase these percentages. It is undoubted that a very liberal supply of floor space, say 160 square feet per patient, is a great protection, and that better results are observed when the heads of the beds are 12 feet apart.

Cubicle Isolation. It is natural that attempts have been made to alter a state of affairs so undesirable. True isolation would demand the provision of a separate room for each patient, but such a plan would not only increase the cost of nursing enormously but would render our present expensively constructed buildings almost useless. More than twelve years ago some wards at the South Western Hospital of the Metropolitan Asylums Board were converted to the cubicle system by the erection of glass partitions which do not reach the roof, each cubicle opening on a central passage down the ward. This arrangement is comparatively economical in nursing, it allows the patients to see each other and even converse over the partitions, and it has been, in Dr. Foord Caiger's experience, most efficacious for the isolation of the less infectious conditions. Each cubicle has a fixed-in basin, water laid on, and separate cloaks for the nurse and medical attendant. More recently wards have been erected, at Sheffield and elsewhere, in which the cubicles have their glass partitions carried to the roof, access being obtained to each from open verandas, no central passage being provided. The isolation so secured is obviously more complete than in the other system, but the difficulties and discomforts of nursing must be much greater, and it must be almost necessary to provide special nurses for delirious patients, who indeed would be a great source of anxiety in any cubicle arrangement.

In carrying out this system, as well as those to be mentioned below, it is necessary that each patient should be provided with a special equipment of brushes, throat instruments, sponge, towels, &c., and that all spoons,

crockery, and so forth should be sterilized after use. The nursing staff, moreover, must be specially trained, and in some hospitals the use of rubber gloves is enjoined. Some authorities appear to doubt whether the overall cloak is necessary, though it would seem wise to insist on the nurses, who have so much more intimate contact with the patient than does the medical attendant, always using it. They will be much less likely to do so if the same precaution is not taken by the doctor. As regards hand washing, some consider that soap and water is quite sufficient and that too much use of antiseptics is apt to crack the skin of the hands and make them more likely to harbour bacteria.

Cubicle wards for the most part appear to have been used experimentally for a limited number of cases only, and different diseases are treated under the same roof. They have, as reports show, been wonderfully successful, it being quite exceptional for a second infection to be contracted in them, the only two diseases likely to give much trouble being chicken-pox and measles. Scarlet fever, rubella, diphtheria, mumps, and whooping-cough have all been treated together in such wards by the same staff of nurses with a minimum of cross infection.

Barrier Nursing, introduced under that name by the late Dr. Biernacki, is an attempt to limit septic infection in a general ward, usually in the case of scarlet fever. The patient is, as it were, isolated in the ward itself, special equipment as in the cubicle system being provided for him, while a cord between two supports at the foot of the bed reminds the nurses that a certain ritual of cloak-wearing and hand-washing must be gone through whenever he is touched. I suppose most of us make use of some such method in the case of patients whom we consider may be dangerous to others.

Bed Isolation. From the isolation of one, or of two or three patients, it is only a step to the isolation of every one in the ward, that is to say the provision of separate utensils and articles for every patient and the adoption of the complete ritual in every case. This seems to have been first carried out systematically by Dr. Crookshank at Mortlake, with very gratifying results, and would appear to be the most rational system for the large fever hospitals to imitate, though in training schools for nurses it would be extremely difficult to secure the accurate and conscientious practice of all the details of the ritual. As mentioned above, the cubicle experiments have been usually limited to one or two wards staffed by specially selected nurses, and, interesting as they are, they have contributed more to our knowledge of the infectivity and means of dissemination of certain diseases than to a solution of the question of how to prevent cross-infection in the

ordinary wards of a fever hospital. Dr. Crookshank's experiment seems to me of more practical utility, and I would place with it Dr. Cameron's isolation treatment of scarlet fever patients at the South Eastern Hospital, and the system employed by Dr. Peters at Bristol, who endeavours to 'isolate' all his cases by carrying out all precautions against contact infection and, in addition, keeps all windows open, top and bottom, even throughout the winter, with a view of preventing possible aerial infection. His success in reducing secondary infections to the very low figure of 0.4 per cent. of his patients and, in particular, in escaping infection in fourteen out of fifteen invasions of chicken-pox appears to me the strongest argument in favour of the probability of aerial convection in that disease yet adduced. If convection currents have been responsible for ward infections, even in cubicle or isolation systems, very free cross-ventilation should theoretically do much to break them up and dissipate the virus, and improvement of results after the introduction of such ventilation certainly points strongly to such a method of infection being possible.

Isolation methods, then, have proved very useful in wards occupied by patients suffering from the same disease. They have been also used by Dr. Rundle at the Liverpool City Hospital in wards containing patients suffering from many distinct infectious conditions. This courageous experiment was remarkably successful, 741 patients being treated with only two instances of cross-infection, both scarlet fever. It must be understood, however, that while measles, chicken-pox, and whooping-cough patients were treated together with cases of diphtheria and scarlet fever, the infectious population of the ward was much diluted, as it were, by the admission of many erysipelas and puerperal cases as well as certain 'observation' cases who turned out to be suffering from no infectious disease at all. Not only does such a method tend to lower the concentration of infection in a ward but it also introduces persons of insusceptible age periods or actually protected by previous attacks. The failure of chicken-pox to spread is certainly noteworthy. A great deal would obviously depend, however, on the stage in which the patients were admitted, as Dr. F. Thomson's recent work suggests that the infectivity does not last much more than a week. Unless measles was admitted occasionally in the prodromal stage, or at least on the first day of the rash, the absence of secondary cases would not be so remarkable.

In experiments of this kind we have to remember the very different degrees of infectivity associated with different diseases. In the old days diphtheria was often treated in the wards of general hospitals and children's hospitals with little or no precaution and for the most part without bad

results. Enteric fever, again, was similarly treated. When I first went as an assistant to our old hospital, diphtheria and enteric fever were, as often as not, treated in one ward, and always by the same staff of nurses. For years our enteric wards have been the common receptacle of cerebro-spinal meningitis, puerperal septicæmia, erysipelas, and pneumonia, and it is hardly necessary to say that such diseases can be treated perfectly safely together without any ritual and with methods of ordinary cleanliness only. In the side-rooms of these wards cases of mumps, rubella, and chicken-pox have been almost constantly treated by the same staff, with very simple extra precautions, and without a single accident.

Dr. Frederic Thomson has subjected the bed isolation system to a more severe test. He has not 'diluted' his infecting or his susceptible cases. He treated in all 457 patients. Among them 256 cases of scarlet fever caused only two cross-infections, 104 diphtheria none, 41 rubella none, 23 mumps one, 75 whooping-cough five. Only 2 cases of measles were treated and both caused secondary infection. Of 63 chicken-pox cases seven appear to have infected others, and Dr. Thomson is of opinion that this disease up to the third day of eruption is airborne.

It will be noticed that by sufficient care and attention, whether in cubicles or in open wards, transmission of the infection of scarlet fever, diphtheria, and rubella can be satisfactorily prevented, but that complete success is far from being attained in the case of chicken-pox and measles. It is only natural that many should have come to the conclusion that these diseases must therefore be transmitted by aerial convection. While we need not go so far as to deny absolutely the possibility of such means of dissemination, it has not been definitely proved even in the case of small-pox, and it is well to remember how most confident assertions regarding the mode of transmission of other diseases have been proved entirely wrong as our knowledge of the diseases in question has increased. We may recollect also that measles and chicken-pox, either from a higher natural infectivity on their part or from a greater natural susceptibility on the part of the average child, are much more likely to cause secondary infections, whether precautions are taken or not. Few susceptibles, indeed, escape under ordinary conditions, a result quite different from that which follows exposure to scarlet fever, diphtheria, or even rubella. I think it quite possible that a less massive dose may be required to produce measles and chicken-pox than is the case in the other diseases named, and that a disinfecting ritual sufficient to prevent the latter might not be equally effective for the former. This of course assumes that the precautions against contact infection never break down; should they do so on one or two occasions, surely it is those diseases

which practically every child contracts which will be transmitted, and not those which many people go through life without taking. Dr. Chapin, who has had considerable success in preventing measles at the Providence Hospital, is inclined, when infection occurs, to assume that the virus of measles is less easily washed from the hands of nurses than is that of scarlet fever. We have no reason to believe the virus lives long, but it may well be very potent for the short time it does so. Lastly, I have never understood what happens in a cubicle or 'bed isolation' ward if a night nurse is attending to one patient and sees a child falling out of bed, or in a convulsion, farther up the ward. Does she always wait to disinfect? The most perfect systems must break down occasionally.

Another problem in these wards is the question of books and toys. None can be allowed if they are not tied to the bed. Dr. Thomson speaks of chocolates being thrown across the ward; the same thing might happen with fruit. The patients themselves must be kept in bed or only allowed up to sit beside their own beds. The practical difficulties are undoubtedly very great and the strain on the staff must be immense. For this reason one has the greatest admiration for those who have confronted these difficulties and have obtained such striking results. But as long as separate wards are available for these cases I think they should be used. On the other hand, bed isolation methods may well be applied in ordinary scarlet fever or diphtheria wards, and I feel that it is by working on these lines, as laid down by Crookshank, Cameron, and Peters, that we shall best secure the safety of the patients in our hospitals. Even this will probably require a considerable increase of staff, and at present, when we are confronted with building schemes for the accommodation of the extra nurses required by the adoption of the eight hours day (our own hospital will require at least fifty more), the outlook is not too hopeful.

AGGRAVATION OF THE PATIENT'S OWN ILLNESS BY SEPTIC INFECTION. While I think that perhaps there is nowadays too great a tendency to assume that, if a patient gets much worse shortly after admission, it is entirely due to hospitalization, it must be readily admitted that occasionally a clean case becomes dangerously septic. But in the vast majority of those cases in which a marked exacerbation of the throat symptoms of a scarlatina patient, for instance (and it is to that disease that the following remarks chiefly refer), takes place within a week of admission, I find that the throat has been noted as 'dirty' or 'patched' on admission, and these are after all merely the first stages of a thoroughly septic condition. On the other hand, many cases of rhinitis, and perhaps of otorrhœa, occurring in convalescence, may be due to septic infection,

and the same may also be true of adenitis. Nevertheless, these complications all occurred before the days of fever hospitals, and some of the worst septic cases which I have seen, both in the acute stage and in convalescence, were treated entirely at home. And, whatever precautions we may think it necessary to take, we cannot hope to do more than diminish the incidence of such complications.

To prevent septic infection spreading from patient to patient what steps should be taken? There are certain disadvantages connected with the routine treatment of the throat and nose of 'clean' cases in hospital wards. If antiseptics are used they may irritate the throat, and, rather than prevent infection, they may increase the liability to it. It is difficult to hold a very favourable opinion of local antiseptic treatment, when we recollect how absolutely powerless it often is to rid the throat of bacilli after an attack of diphtheria. Are we, then, to follow those who douche the throat and nose daily with sterile water? The mechanical effect of such a procedure may be useful, and it is at least not irritating, nor is it likely to cause otitis, if too great a pressure of water is avoided. But before adopting it we must be certain that the nozzles of the douches are above suspicion; otherwise they might be likely to carry infection from septic to clean cases. It may well be the case that in busy hospitals, where inexperienced probationers have to carry out much of the routine treatment of the milder cases, there is some risk in systematic douching, and therefore, if a case is 'clean', it is well to leave it alone.

An application of the methods of barrier nursing or bed isolation as described above, and very free ventilation of the wards will no doubt do much to prevent any aggravation of the patient's condition. Ample floor space per patient is probably as important as anything else.

In our convalescent wards I try to isolate all cases of rhinitis in the side-rooms, and they are not allowed to mix with the other patients. The complication has become much less frequent since this precaution was adopted. As regards otorrhœa, the patients are allowed to remain in the general wards, but the ears are kept loosely plugged with cotton-wool, covered with a light pad of wool, and a helmet bandage is applied over all. There is no fear, then, of other patients becoming contaminated with the discharge, or of the latter soiling the pillows and drying there. The adoption of this plan is also wise with a view of limiting 'return' cases, which are caused most frequently by patients who have suffered from septic discharges.

'RETURN CASES'. When a patient discharged from a fever hospital infects, or is suspected of infecting, another person, the latter is termed

a 'return case'. Such cases, as a rule, occur only after scarlatina and diphtheria. I have never seen them follow the discharge from hospital of patients who have suffered from other infections. As regards diphtheria, moreover, return cases are not common in Edinburgh. The convalescent from scarlatina, however, is very liable to infect others on his dismissal, and return cases occur in connexion with all fever hospitals, and in the present state of our knowledge appear likely to continue to do so.

As might be expected, hospital authorities have been extremely anxious to abolish this slur on their efficiency, and many investigations of the subject have been made. Of these the most important, as referring to by far the largest number of cases, are those undertaken on behalf of the Metropolitan Asylums Board. Professor Simpson reported in 1899 that about half the number of supposed return cases were really due to patients leaving the hospitals in an infectious condition; that these constituted at least 1·6 per cent. of the total discharges; that 80 per cent. of the infecting cases suffered from discharges from the mucous membranes (nose, throat, or ear); that 'return cases' are not due to premature dismissal from hospital, and the isolation in hospital is if anything too long; and, lastly, that the warm baths, customarily given immediately before the patient is discharged, do not remove the infection, but contribute to its increase.

In 1904 Dr. Cameron, who had made a further investigation, reported that the supposed infecting cases were 4·1 per cent. of the total number discharged from hospital, and that the majority were probably the actual cause of the 'return cases'. He considered that, although many of these infecting cases had been detained beyond the average time in hospital, length of detention is not in itself the cause of their infectiousness. Like Professor Simpson, he held that the principal cause of the occurrence of 'return cases' is the persistence and recurrence of mucous discharges from the nose, and that these occur particularly during the winter months. In his view infection is retained longer by patients who are treated in hospital, and that this is due to infection with micro-organisms from other patients. He reported further that late desquamation cannot be regarded as evidence of infectivity, and recommended that, during the winter, the warm bath on dismissal should be given the night before. The general conclusion was that under the present conditions of hospital treatment it is impossible to avoid the occurrence of 'return cases' altogether, but that something can be done by more isolation and more asepsis in hospital.

As regards return cases of diphtheria, they may occur, not only after a diphtheria patient has been dismissed from hospital, but also after the

discharge of scarlatina patients. Dr. Cameron found that 1·2 per cent. of the total diphtheria cases and 0·35 per cent. of the scarlatina cases were, after their discharge from hospital, supposed to have infected persons with diphtheria. He recommended that bacteriological examinations should be made of both throat and nose before the patient leaves hospital, the return cases, like those of scarlatina, being associated with morbid conditions of the nose in the infecting individuals.

The conclusions of Dr. Cameron were commented on by the Medical Superintendents of the Metropolitan Asylums Board, who made, as regards scarlatina, certain recommendations. These include the advisability of early transference of the patients to convalescent wards, the establishment of a discharge ward in which patients, after their bath, can pass their last night in hospital, and the encouragement of the patients to be as much as possible in the open air. They also suggested that printed instructions should be given to the parents of discharged children, advising that some degree of isolation be maintained for three weeks at home. The cubicle wards now fitted in some of the Board's hospitals are also the result of their recommendations.

In Edinburgh we dispense with the warm bath just before dismissal. It is easy to see how on a cold winter day a slight nasal catarrh is very readily lit up by such a procedure, and how a patient who leaves hospital with a dry clean nose may, on his arrival home, be suffering from nasal discharge. Such a catarrhal discharge will often become purulent, and, in any case, it is likely to be highly infectious. We also give a printed card of instructions to the parents of each discharged patient, suggesting that the child should occupy a separate bed for at least a week, and, if possible, a separate room. Warning against kissing, and playing with susceptible children, for the same period is also given, and the advisability of keeping the child in the open air as much as possible is emphasized. It is also recommended that special crockery and utensils be used for the discharged patient.

Except in special circumstances it has been my custom to detain scarlatina patients for six weeks, and at the end of that time to dismiss them if they are not suffering from rhinitis, otorrhœa, or other discharges. When accommodation is short, detention is occasionally reduced to five weeks without any bad result, and desquamation is disregarded. In connexion with this, some figures given by Dr. Matthews are of interest. He found that of 2,213 cases who still showed desquamation at the date of their discharge from the Northern Hospital, 49, or 2·21 per cent., caused 'return cases' as against 2·12 per cent. of 1,931 patients who had completed their peeling. This difference is too slight to be regarded seriously, and goes far to prove that

detention for desquamation alone is quite unnecessary. Of cases with rhinitis and otorrhœa 2·68 per cent. caused infection, and when analysed it appeared that of those with rhinitis 3·20 per cent., as against 0·96 per cent. for patients suffering from otorrhœa, were responsible for 'return cases'. It may be added that those hospital physicians who disregard desquamation and who have adopted a shorter period of detention than six weeks are satisfied that the number of 'return cases' is not increased by this procedure. Dr. Moore, for instance, reports that in Huddersfield the percentage of infecting cases during the period that patients were detained until desquamation was completed was 4·8, whereas, since this procedure has been dropped, the infecting cases were reduced to 4 per cent. Under the old system the average detention in hospital was 44·3 days, under the new it fell to twenty-nine days. The economy effected by this reduction of the period of isolation must, therefore, be very considerable, and the statistics of Huddersfield, Leicester, and Southampton suggest that 'return cases' are at least not increased. At the last named, indeed, Dr. Lauder in 1914 was able to report 589 cases treated in three years, with a minimum detention of twenty-eight days, an average of thirty-two to thirty-six days, and not a single return case.

I have recently had the opportunity of comparing the effects of short and long periods of detention in patients treated in the same wards and under precisely similar conditions. Three years ago the Admiralty commandeered the Leith Fever Hospital for war purposes, and its patients have since been accommodated with us. For some years Dr. Robertson had adopted a four weeks' minimum detention and, when he transferred his patients to me, I saw no reason to change his routine practice. For the last three years, therefore, our Edinburgh patients have been discharged after our ordinary minimum detention of six weeks, while the Leith ones have been discharged on an average two weeks earlier. In both groups any patient with complications or discharges was detained as usual, in some instances for long periods, and it may be mentioned that 4 out of 21 Leith infecting cases had been in hospital over seven weeks. The results of both groups combined were worse than those of recent years, a fact I attribute partly to the frequent changes of staff and the overwork caused by the war. Of 2,561 cases treated the infecting rate was 3·5 per cent., of 1,829 Edinburgh cases 3·7 and of 732 Leith cases 2·8 per cent. In seven previous years the percentage had varied between 1·5 and 3, and was usually about 2·5, so neither result can be called satisfactory, but as a comparison between two methods, carried out under exactly similar conditions and over a sufficient period of time, the experience is not without interest and does not

support the views of those who still believe in the infectivity of desquamation. Many of the Leith patients left us with the skin of their hands hanging in rags. It may be added that the boundaries between Edinburgh and Leith are purely artificial. They form a single community and, if anything, the conditions of housing and life in Leith are worse.

The time limit allowed for the 'return case' to occur is six weeks. As a matter of fact, few patients suspected of being infected by a discharged case come in after a longer interval. None such have been admitted to the City Hospital recently, and I therefore regard the interval as sufficient.

It must be, of course, remembered that the 'return case' has not necessarily been infected by the patient discharged. It is curious how often a patient is admitted ten days, a week, or even a few days *before* the first case from the same house is discharged. Twice within a period of six weeks a patient was admitted on the very day a member of the same family was to return home. It is obvious that, had these persons been infected only a few days later, the hospital would have been regarded as responsible. Such occurrences point to imperfect disinfection of the houses, to the parents concealing from the sanitary officials articles of clothing and books used by the first patient, to carriers or missed cases remaining in the house, and to mere coincidence, the second patient having picked up his infection at school or elsewhere. Indeed, many of the 'return cases' in Edinburgh attended schools in which scarlatina was prevalent at the time. Whether we can go so far as Professor Simpson, and say that only half the alleged infecting cases are really responsible is very doubtful, but that many cases are due to coincidence there can be no question, and it is interesting to note that the 'return rate', as a rule, rises when there is undue epidemic prevalence of the disease, that is, when the chances of infection from other sources are much increased. Lastly, it must be recollected that 'return cases' are not a hospital phenomenon. Dr. Nash and other authorities find that there is a higher percentage of 'returns' in cases treated at home.

In conclusion, it may be stated that a certain number of return cases will probably continue to occur in spite of all precautions, and that they will be most frequently noticed in the winter months, and when the climatic conditions favour catarrhal conditions. Still, I believe that much may be done by the use of convalescent wards, the isolation of septic cases, and the employment of the disinfecting bath the night before discharging the patient. As regards the personal disinfection much care must be taken, attention being particularly paid to the hair. The particular disinfectant employed is a matter of small moment. The real danger lies in the faucial

and nasal mucous membranes, and as, unfortunately, we cannot treat these as we do the clothes, and submit them to steam disinfection, perfect safety cannot, in the present state of our knowledge, be expected. Isolation for even twenty-four hours before dismissal is a step in the right direction, and this is ensured by giving the bath the night before. I have tried the experiment of a week's isolation after passing through the discharging house in the ordinary way, but with only slight success, as for 200 cases the infecting rate was 3 per cent. Not infrequently, moreover, did return cases occur after patients had been kept in our convalescent home at Musselburgh for a fortnight after their discharge from hospital. Such facts show the great difficulties of the question, but, until we learn something definite about the bacteriology of scarlatina, we must content ourselves with working on the lines indicated above, and be not too much disappointed if we cannot attain complete success.

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